Direct Substitution of Arylalkynyl Carbinols Provides Access to Diverse Terminal Acetylene Building Blocks

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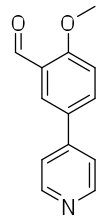
The ^{1}H and ^{13}C NMR spectra were recorded on Bruker instruments at 500 MHz. Chemical shifts are reported in ppm and are referenced to residual $CHCl_3$ solvent; 7.24 and 77.23 ppm for ^{1}H and ^{13}C, residual solvent MeOH; 4.78, 3.31 and 49.15 ppm respectively. The high-resolution mass spectrometry was provided by University of Connecticut Mass Spectrometry Laboratory using AccuTOF mass spectrometer and/or using DART source. IR data were obtained using Alpha diamond ATR probe. TLC analyses were performed on Sorbent Technologies silica gel HL TLC plates. All glassware was oven-dried and allowed to cool under an argon atmosphere. Anhydrous dichloromethane, and tetrahydrofuran were used directly from Baker Cycle-Tainers. All reagents were used directly from commercial sources unless otherwise stated. Boronic acids for Suzuki coupling were purchased from Frontier Scientific, Inc, AK Scientific, Sigma Aldrich. The top B ring aromatic (a) 5-bromo-2-methoxybenzaldehyde and 3-formyl-4-methoxyphenylboronic acid were purchased commercially from Sigma Aldrich and AK Scientific , (b) 3-bromo-5-methoxybenzaldeyde and (c) 7-bromobenzo[d][1,3]dioxole-5-carbaldehyde were synthesized according to the literature[1,2] (d) 3-bromo-4,5-dimethoxybenzaldehyde was obtained by the methylation of vanillin[3].

General procedure for the Suzuki Coupling

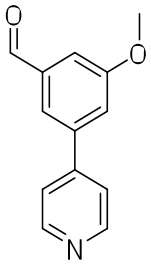
An oven dried 100 mL pressure vessel with stir bar was cooled to room temperature under argon. Bromo benzaldehyde, boronic acid and Cs_2CO_3 in anhydrous dioxane were stirred and purged under argon for 15 minutes. $Pd(PPh_3)_2Cl_2$ was then added and purging continued for further 10 minutes. The pressure vessel was sealed with a screw cap and placed in a preheated oil bath at 80 °C for 12 h. The dark colored reaction mixture was cooled, diluted with ether, filtered through celite and rinsed with ether. The filtered solution was concentrated, diluted with CH_2Cl_2, pre-absorbed onto silica gel and purified by column chromatography.

2-methoxy-5-(pyridin-4-yl) benzaldehyde (1a)



According to the general Suzuki coupling procedure bromo aldehyde (3.50 g, 16.5 mmol), pyridine-4-boronic acid (4.05 g, 32.9 mmol), Cs_2CO_3 (16.1 g, 4.93 mmol), $Pd(PPh_3)_2Cl_2$ (1.16 g, 1.65 mmol, 10 mol% Pd) and anhydrous dioxane (16.5 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 60 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (3.90 g, 85%): TLC R_f = 0.13 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.60 (d, J = 6.0 Hz, 2H), 8.09 (d, J = 2.4 Hz, 1H), 7.81 (dd, J = 8.7, 2.4 Hz, 1H), 7.44 (d, J = 6.0 Hz, 2H), 7.07 (d, J = 8.7 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 162.5, 150.5, 146.7, 134.2, 130.6, 127.0, 125.3, 121.1, 112.7, 56.1; IR (neat cm^{-1}) 3063, 2976, 2896, 1677,1603, 1271, 804, 504; HRMS (DART, $M^+ + H$) *m/z* 214.0886 (calculated for $C_{13}H_{12}NO_2$, 214.0868).

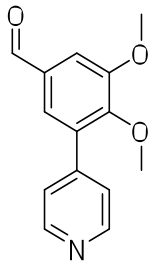
3-methoxy-5-(pyridin-4-yl) benzaldehyde (1b)



According to the general Suzuki coupling procedure bromo aldehyde (1.70 g, 7.91 mmol), pyridine-4-boronic acid (1.94 g, 15.8 mmol), Cs_2CO_3 (7.72 g, 23.7 mmol), $Pd(PPh_3)_2Cl_2$ (0.55 g,

23.7 mmol, 10 mol% Pd) and anhydrous dioxane (8 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 20 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (1.38 g, 82%): TLC R_f = 0.2 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.66 (d, J = 5.0 Hz, 2H), 7.67 (s, 1H), 7.48 (d, J = 5.0 Hz, 2H), 7.41 (s, 1H), 7.37 (s, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7, 160.9, 150.7, 146.9, 140.7, 138.7, 121.8, 119.9, 112.9, 100.1, 55.9; IR (neat cm^{-1}) 3013, 2972, 2834, 1693, 1586, 1468, 1217, 1151, 1046, 852, 816; HRMS (DART, M^+ + H) *m/z* 214.0897 (calculated for $C_{13}H_{12}NO_2$, 214.0868).

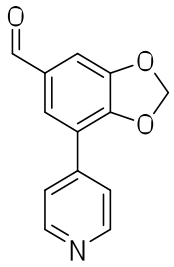
3,4-dimethoxy-5-(pyridin-4-yl)benzaldehyde (1c)



According to the general Suzuki coupling procedure bromo aldehyde (1.06 g, 4.33 mmol), pyridine-4-boronic acid (1.06 g, 8.65 mmol), Cs_2CO_3 (4.22 g, 12.98 mmol), $Pd(PPh_3)_2Cl_2$ (0.30 g, 0.43 mmol, 10 mol% Pd) and anhydrous dioxane (4.3 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 30 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale yellow solid (0.84 g, 80%): TLC R_f = 0.2 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.66 (d, J = 6.0 Hz, 2H), 7.49 (d, J = 2.0 Hz, 1H), 7.45 – 7.44 (m, 3H), 3.96 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 154.0, 152.2, 150.1, 145.1, 133.5, 132.8, 126.4, 124.1, 111.2, 61.3, 56.4; IR (neat cm^{-1})

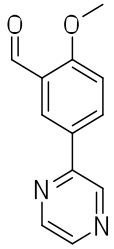
3058, 3016, 2838, 2708, 1692, 1579, 1460, 1297, 1048, 816; HRMS (DART, $M^+ + H$) *m/z* 244.0999 (calculated for $C_{14}H_{14}NO_3$, 244.0974).

7-(pyridin-4-yl)benzo[d][1,3]dioxole-5-carbaldehyde (1d)



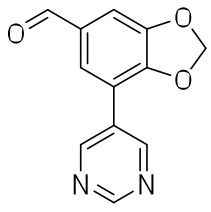
According to the general Suzuki coupling procedure bromo aldehyde (3.04 g, 13.3 mmol), pyridine-4-boronic acid (3.26 g, 26.6 mmol), K_3PO_4 (4.80 g, 22.6 mmol), $Pd_2(dba)_3$ (1.21 g, 1.32 mmol, 10 mol% Pd), PCy_3 (1.11 g, 3.90 mmol) and anhydrous dioxane (36 mL), H_2O (17 mL) was heated at 100 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 60 g, 50% EtOAc/hexanes) biaryl ketone **10** was obtained as a pale white solid (2.41 g, 80%): TLC R_f = 0.2 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.69 (d, J = 6.0 Hz, 2H), 7.67 – 7.64 (m, 3H), 7.36 (s, 1H), 6.18 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 150.8, 150.6, 149.7, 142.0, 132.5, 127.0, 122.2, 120.0, 107.5, 102.8; IR (neat cm^{-1}) 3337, 3062, 2915, 1685, 1594, 1402, 1097, 891; HRMS (DART, $M^+ + H$) *m/z* 228.0689 (calculated for $C_{13}H_{10}NO_3$, 228.0661).

2-methoxy-5-(pyrazin-2-yl) benzaldehyde (1e)



According to the general Suzuki coupling procedure iodopyrazine (1.11 g, 5.39 mmol), 3-formyl-4-methoxyphenylboronic acid (1.94 g, 10.8 mmol), Cs_2CO_3 (5.27 g, 16.2 mmol), $Pd(PPh_3)_2Cl_2$ (0.40 g, 0.54 mmol, 10% Pd) and anhydrous dioxane (6 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 30 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (0.84 g, 73%): TLC R_f = 0.3 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.49 (s, 1H), 9.01 (s, 1H), 8.57 (s, 1H), 8.45 (dd, J = 9.3, 2.1 Hz, 2H), 8.29 (dd, J = 8.7, 2.1 Hz, 1H) 7.12 (d, J = 8.8 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 163.1, 151.5, 144.3, 143.0, 141.8, 134.5, 129.2, 127.1, 125.2, 112.7, 56.2; IR (neat cm^{-1}) 3055, 2980, 2884, 1675, 1604, 1454, 1414, 1392, 1272, 1256, 1112, 1010, 825, 512; HRMS (DART, M^+ + H) *m/z* 215.0831 (calculated for $C_{12}H_{11}N_2O_2$, 215.0821).

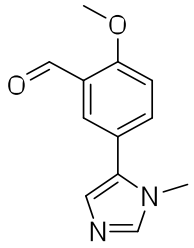
7-(pyrimidin-5-yl) benzo[d][1,3]dioxole-5-carbaldehyde (1f)



Bromo aldehyde (0.8 g, 3.49 mmol), pyrimidine-5-boronic acid (0.86 g, 6.99 mmol), K_3PO_4 (1.26 g, 5.94 mmol), $Pd_2(dba)_3$ (0.32 g, 0.35 mmol, 10% Pd), PCy_3 (0.29 g, 1.05 mmol) anhydrous dioxane (9.4 mL), H_2O (4.7 mL) was heated at 100 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 20 g, 50% EtOAc/hexanes) biaryl aldehdye was obtained as a pale white solid (0.58 g, 73%): TLC R_f = 0.3 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 9.21 (s, 1H), 9.10 (s, 2H), 7.62 (d, J = 1.5 Hz, 1H), 7.39 (d, J = 1.5 Hz, 1H), 6.19 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 158.2, 155.6, 150.6, 149.7, 132.9,

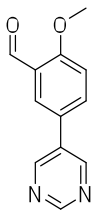
128.8, 126.3, 116.2, 107.9, 102.9; IR (neat cm^{-1}) 3062, 2919, 2795, 1682, 1411, 1253, 1091, 933, 720; HRMS (DART, $M^+ + H$) *m/z* 229.0628 (calculated for $C_{12}H_9N_2O_3$, 229.0613).

2-methoxy-5-(1-methyl-1H-imidazol-5-yl) benzaldehyde (1g)



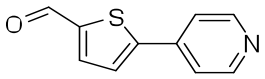
According to the general Suzuki coupling procedure 5-bromo-1-methyl-1H-imidazole (1.05 g, 6.50 mmol), 3-formyl-4-methoxyphenyl boronic acid (1.75 g, 9.75 mmol), sat. Na_2CO_3 (3.25 mL), $PdCl_2$dppf (0.095 g, 0.130 mmol, 2 mol% Pd) and anhydrous ethanol (30 mL), toluene (5 mL) was heated at 85 °C for 2 h. Following the general workup and flash chromatography (SiO_2, 20 g, 3%MeOH/CH_2Cl_2) biaryl aldehyde was obtained as an orange solid (0.98 g, 70%): TLC R_f = 0.06 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.47 (s, 1H), 7.81 (d, *J* = 2.1 Hz, 1H), 7.56 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.51 (br s, 1H), 7.06 - 7.05 (m, 2H), 3.96 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 162.5, 139.1, 135.9, 132.0, 128.3, 128.1, 125.1, 122.8, 112.4, 55.9, 32.3; IR (neat cm^{-1}) 3101, 2971, 2945, 2860, 2768, 1681, 1614, 1482, 1245, 1114, 1017, 827; HRMS (DART, $M^+ + H$) *m/z* 217.0998 (calculated for $C_{12}H_{13}N_2O_2$, 217.0977).

2-methoxy-5-(pyrimidin-5-yl)benzaldehyde (1h)



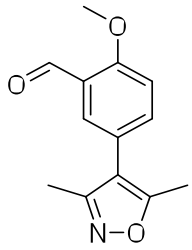
According to the general Suzuki coupling procedure bromo aldehyde (1.50 g, 6.97 mmol), pyrimidine-5-boronic acid (1.73 g, 13.9 mmol), Cs_2CO_3 (6.81 g, 20.9 mmol), $Pd(PPh_3)_2Cl_2$ (0.49 g, 0.70 mmol, 10 mol% Pd) and anhydrous dioxane (5 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 30 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (1.04 g, 70%): TLC R_f = 0.2 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.51 (s, 1H), 9.18 (s, 1H), 8.93 (s, 2H), 8.06 (d, J = 2.3 Hz, 1H), 7.77 (dd, J = 8.7, 2.3 Hz, 1H), 7.15 (d, J = 8.7 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 162.5, 157.7, 154.7, 134.2, 133.2, 127.1, 127.0, 125.6, 113.1, 56.2; IR (neat cm^{-1}) 3035, 2849, 2760, 1742, 1606, 1498, 1414, 1387, 1186, 1014, 722; HRMS (DART, M^+ + H) *m/z* 215.0841 (calculated for $C_{12}H_{11}N_2O_2$, 215.0821).

5-(pyridin-4-yl) thiophene-2-carbaldehyde (1i)



According to the general Suzuki coupling procedure bromo aldehyde (0.56 g, 2.93 mmol), pyridine-4-boronic acid (0.72 g, 5.86 mmol), Cs_2CO_3 (2.86 g, 8.79 mmol), $Pd(PPh_3)_2Cl_2$ (0.21 g, 0.30 mmol, 10 mol% Pd) and anhydrous dioxane (5 mL) was heated at 80 °C for 12 h. Following the general workup and flash chromatography (SiO_2, 20 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (0.44 g, 80%): TLC R_f= 0.2 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.66 (d, J = 4.6 Hz, 2H), 7.76 (d, J = 3.9 Hz, 1H), 7.55 (d, J = 3.9 Hz, 1H), 7.50 (d, J = 4.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.9, 151.0, 150.3, 144.4, 140.2, 137.1, 126.2, 120.4; IR (neat cm^{-1}) 3304, 3091, 1713, 1415, 1214, 1047, 799; HRMS (DART, M^+ + H) *m/z* 190.0351 (calculated for $C_{10}H_8NOS$, 190.0327).

5-(3,5-dimethylisoxazol-4-yl)-2-methoxybenzaldehyde (1j)



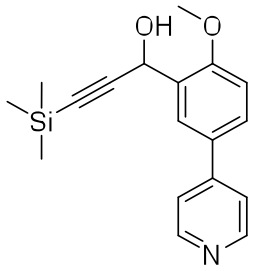
According to the general Suzuki coupling procedure 4-iodo-3,5-dimethylisoxazole (1.14 g, 5.10 mmol), 3-formyl-4-methoxyphenyl boronic acid (4.50 g, 25.5 mmol), Na_2CO_3 (3.50 g, 33.1 mmol), $Pd(PPh_3)_4$ (0.12 g, 0.10 mmol, 2 mol% Pd), anhydrous dioxane (75 mL), H_2O (17 mL) was heated at 85 °C for 2 h. Following the general workup and flash chromatography (SiO_2, 30 g, 50% EtOAc/hexanes) biaryl aldehyde was obtained as a pale white solid (1.04 g, 88%): TLC R_f= 0.6 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.5 (s, 1H), 7.68 (d, J = 2.2 Hz, 1H), 7.41 (dd, J = 8.6, 2.2 Hz, 1H), 7.05 (d, J = 8.6 Hz, 1H), 3.95 (s, 3H), 2.35 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.5, 165.5, 161.3, 158.7, 137.0, 129.0, 125.2, 123.2, 115.5, 112.5, 56.1, 11.7, 10.9; IR (neat cm^{-1}) 3038, 2923, 2862, 2724, 1682, 1601, 1268, 1120, 1014, 825; HRMS (DART, $M^+ + H$) *m/z* 232.0993 (calculated for $C_{13}H_{14}NO_3$, 232.0976).

General Procedure for Alkyne Addition

A 50 mL flask with stir bar was flame dried under argon. Ethynyltrimethyl silane was added to 2M THF at 0 °C and stirred for 2 minutes. Isopropyl magnesium chloride was added dropwise and stirred initially at 0 °C for 30 minutes followed by another 30 minutes at room temperature. The grey colored Grignard reagent was cooled to 0 °C and the aldehyde in (0.1 M) THF was added dropwise for 5 minutes. The reaction was followed by TLC and quenched with sat. NH_4Cl. The organic layer was separated and water layer extracted 3 times with ether. The

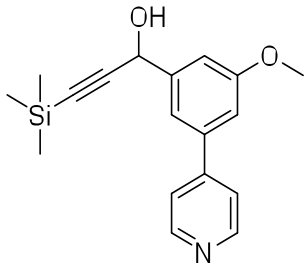
combined organic extracts were dried with $MgSO_4$ filtered and evaporated. The crude compound was pre-absorbed onto silica gel and purified by column chromatography.

1-(2-methoxy-5-(pyridin-4-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10a)



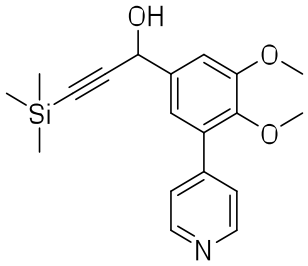
According to the general nucleophilic addition ethynyltrimethyl silane (6.6 mmol, 0.93 mL) in THF (2 M, 3.29 mL) and isopropyl magnesium chloride (2 M, 3.3 mL) was stirred. At 0 °C was added the aldehyde (5.06 mmol, 1.07 g) in THF (0.1 M, 50 mL).Following the general workup and flash chromatography (SiO_2, 40 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a white solid (1.48 g, 94%): TLC R_f = 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, J = 5.7 Hz, 2H), 7.91 (d, J = 2.2 Hz, 1H), 7.58 (dd, J = 8.5, 2.2 Hz, 1H), 7.44 (d, J = 6.0 Hz, 2H), 6.98 (d, J = 8.5 Hz, 1H), 5.77 (s, 1H), 3.92 (s, 3H), 0.19 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 150.3, 148.0, 130.5, 129.8, 128.3, 127.0, 121.2, 111.6, 104.7, 91.5, 61.0, 56.0, 0.1; IR (neat cm^{-1}) 3139, 2977, 2868, 2165, 1562, 1504, 1228, 1011; HRMS (DART, M^+ + H) *m/z* 312.1393 (calculated for $C_{18}H_{22}NO_2Si$, 312.1420).

1-(3-methoxy-5-(pyridin-4-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10b)



According to the general nucleophilic addition ethynyltrimethyl silane (2.1 mmol, 0.3 mL) in THF (2M, 1.0 mL) and isopropyl magnesium chloride (2M, 1.0 mL) was stirred. At 0 °C was added the aldehyde (1.7 mmol, 0.4 g) in THF (0.1M, 17 mL).Following the general workup and flash chromatography (SiO_2, 20 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a brownish oil (0.51 g, 94%): TLC R_f= 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (br s, 2H), 7.46 (d, J = 4.5 Hz, 2H), 7.38 (s, 1H), 7.19 (s, 1H), 7.07 (s, 1H), 5.50 (s, 1H), 3.85 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 150.1, 148.5, 143.5, 139.7, 122.0, 118.0, 113.1, 112.7, 105.4, 91.7, 64.7, 55.7, 0.0; IR (neat cm^{-1}) 3153, 2958, 2899, 2837, 2170, 1648, 1550, 1325, 1217, 1049; HRMS (DART, M^+ + H) *m/z* 312.1434 (calculated for $C_{18}H_{22}NO_2Si$, 312.1420).

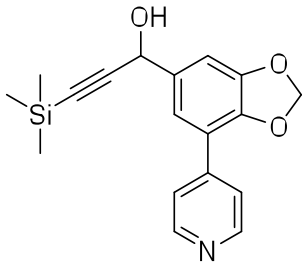
1-(3,4-dimethoxy-5-(pyridin-4-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10c)



According to the general nucleophilic addition ethynyltrimethyl silane (3.79 mmol, 0.54 mL,) in THF (2M, 1.9 mL) and isopropyl magnesium chloride (2M, 1.9 mL) was stirred. At 0 °C was added the aldehyde (2.5 mmol, 0.6 g) in THF (0.1M, 25 mL).Following the general workup and flash chromatography (SiO_2, 30 g, 50% 3%MeOH/CH_2Cl_2) alkynol was obtained as a colorless oil (0.82g, 95%): TLC R_f= 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J = 5.0 Hz, 2H), 7.45 (d, J = 6.0 Hz, 2H), 7.21 (d, J = 1.8 Hz, 1H), 7.09 (d, J = 1.8 Hz, 1H), 5.45 (s, 1H), 3.91 (s, 3H), 3.59 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 149.5, 146.7,

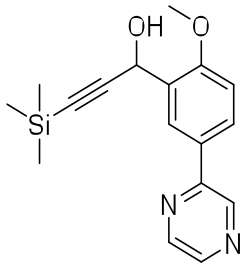
146.4, 137.3, 132.6, 124.3, 120.4, 111.7, 105.5, 91.8, 64.6, 61.0, 56.2, 0.0; IR (neat cm^{-1}) 3085, 3009, 2964, 2821, 2162, 1642, 1410, 1241, 1134, 1049, 828; HRMS (DART, $M^+ + H$) *m/z* 342.1516 (calculated for $C_{19}H_{24}NO_3Si$, 342.1525)

1-(7-(pyridin-4-yl) benzo[d][1,3] dioxol-5-yl)-3-(trimethylsilyl) prop-2-yn-1-ol (10d)



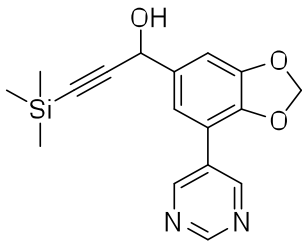
According to the general nucleophilic addition ethynyltrimethyl silane (3.78 mmol, 0.53 mL) in THF (0.53 mL) and isopropyl magnesium chloride (2M, 1.9 mL) was stirred. At 0 °C was added the aldehyde (1.26 mmol, 0.30 g) in THF (0.1M, 12.6 mL).Following the general workup and flash chromatography (SiO_2, 15 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a yellow hygroscopic solid (0.41 g, 99%): TLC R_f= 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.3 Hz, 2H), 7.61 (d, *J* = 5.8 Hz, 2H), 7.28 (s, 1H), 7.09 (s, 1H), 6.05 (s, 2H), 5.42 (s, 1H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.0, 148.8, 145.6, 143.6, 135.9, 122.3, 119.2, 119.0, 108.3, 105.4, 101.8, 91.6, 64.5, 0.0; IR (neat cm^{-1}) 3140, 2958, 2896, 2170, 1639, 1600, 1402, 1248, 1195, 1044, 1002, 824; HRMS (DART, $M^+ + H$) *m/z* 326.1223 (calculated for $C_{18}H_{20}NO_3Si$, 326.1212).

1-(2-methoxy-5-(pyrazin-2-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10e)



According to the general nucleophilic addition ethynyltrimethyl silane (1.45 mmol, 0.20 mL) in THF (2 M, 0.72 mL) and isopropyl magnesium chloride (2 M, 0.72 mL) was stirred. At 0 °C was added the aldehyde (0.90 mmol, 0.20 g) in THF (0.1 M, 9.70 mL). Following the general workup and flash chromatography (SiO_2, 10 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a white solid (0.27 g, 95%): TLC R_f = 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.58 (m, 1H), 8.43 (d, J = 2.4 Hz, 1H), 8.28 (d, J = 2.2 Hz, 1H), 8.01 (dd, J = 8.6, 2.3 Hz, 1H), 7.01 (d, J = 8.6 Hz, 1H), 5.75 (s, 1H), 3.94 (s, 3H), 0.20 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 152.5, 144.3, 142.4, 141.7, 129.6, 129.1, 128.7, 127.0, 111.6, 104.5, 91.7, 61.5, 56.1, 0.1; IR (neat cm^{-1}) 3055, 2980, 2884, 2847, 1913, 1675, 1604, 1414, 1272, 1166, 1112, 1010, 825; HRMS (DART, M^+ + H) *m/z* 313.1394 (calculated for $C_{17}H_{21}N_2O_2Si$, 313.1372).

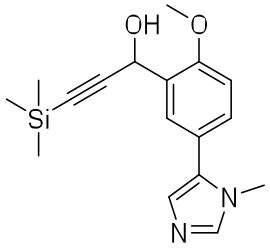
1-(7-(pyrimidin-5-yl) benzo[d][1,3] dioxol-5-yl)-3-(trimethylsilyl) prop-2-yn-1-ol (10f)



According to the general nucleophilic addition ethynyltrimethyl silane (0.90 mmol, 0.14 mL) in THF (2M, 0.5 mL) and isopropyl magnesium chloride (2M, 0.99 mmol, 0.5 mL was stirred. At 0

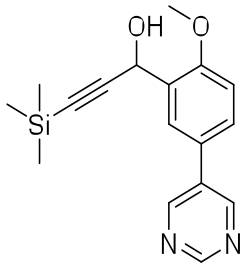
°C was added the aldehyde (0.66 mmol, 0.15 g) in THF (0.1M, 6.6 mL).Following the general workup and flash chromatography (SiO_2, 10 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a light yellow solid (0.21 g, 96%): TLC R_f= 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (s, 1H), 9.05 (s, 2H), 7.24 (s, 1H), 7.10 (s, 1H), 6.07 (s, 2H), 5.42 (s, 1H), 0.20 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 155.5, 148.9, 145.5, 136.0, 129.8, 118.8, 115.3, 108.3, 104.8, 102.0, 92.3, 64.7, 0.0; IR (neat cm^{-1}) 3189, 2955, 2899, 2172, 1606, 1409, 1249, 1041, 1006, 837; HRMS (DART, M^+ + H) *m/z* 327.1190 (calculated for $C_{17}H_{19}N_2O_3Si$, 327.1165).

1-(2-methoxy-5-(1-methyl-1H-imidazol-5-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10g)



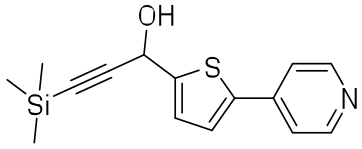
According to the general nucleophilic addition ethynyltrimethyl silane (2.0 mmol, 0.3 mL) in THF (1.0 mL) and isopropyl magnesium chloride (2M, 2.0 mmol, 1.0 mL) was stirred. At 0 °C was added the aldehyde (1.7 mmol, 0.4 g) in THF (0.1M, 16 mL). Following the general workup and flash chromatography (SiO_2, 10 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a light yellow solid (0.49 g, 94%): TLC R_f= 0.03 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.1 Hz, 1H), 7.45 (s, 1H), 7.27 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.98 (s, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 5.76 (s, 1H), 3.88 (s, 3H), 3.60 (s, 3H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 138.8, 133.2, 129.9, 129.6, 128.5, 127.5, 122.3, 111.3, 105.0, 90.9, 60.5, 55.9, 32.6, 0.1; IR (neat cm^{-1}) 3113, 2957, 2899, 2837, 2167, 1488, 1279, 1040, 838; HRMS (DART, M^+ + H) *m/z* 315.1532 (calculated for $C_{17}H_{23}N_2O_2Si$, 315.1529).

1-(2-methoxy-5-(pyrimidin-5-yl) phenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10h)



According to the general nucleophilic addition ethynyltrimethyl silane (3.55 mmol, 0.50 mL) in THF (2M, 1.78 mL) and isopropyl magnesium chloride (2M, 3.55 mmol, 1.78 mL) was stirred. At 0 °C was added the aldehyde (2.37 mmol, 0.51 g) in THF (0.1M, 23.6 mL). Following the general workup and flash chromatography (SiO_2, 20 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a white solid (0.7 g, 95%): TLC R_f = 0.1 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.90 (s, 2H), 7.85 (d, J = 2.2 Hz, 1H), 7.52 (dd, J = 8.4, 2.3 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 5.77 (s, 1H), 3.93 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 157.2, 154.6, 134.0, 130.1, 128.4, 126.9, 126.9, 112.0, 104.2, 91.9, 61.1, 56.1, 0.1; IR (neat cm^{-1}) 3177, 3010, 2837, 2164, 1608, 1308, 1059; HRMS (DART, M^+ + H) *m/z* 313.1391 (calculated for $C_{17}H_{21}N_2O_2Si$, 312.1372).

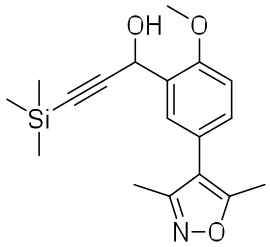
1-(5-(pyridin-4-yl) thiophen-2-yl)-3-(trimethylsilyl) prop-2-yn-1-ol (10i)



According to the general nucleophilic addition Ethynyltrimethyl silane (2.6 mmol, 0.4 mL) in THF (2M, 1.3 mL) and isopropyl magnesium chloride (2M, 2.6 mmol, 1.3 mL) was stirred. At 0 °C was added the aldehyde (2.2 mmol, 0.41 g) in THF (0.1M, 21.6 mL). Following the general

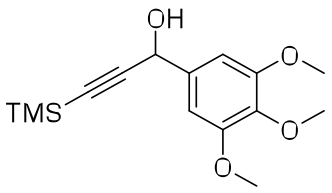
workup and flash chromatography (SiO_2, 20 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a brown solid (0.6 g, 95%): TLC R_f = 0.2 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, J = 6.2 Hz, 2H), 7.41 (d, J = 6.2 Hz, 2H), 7.33 (d, J = 3.7 Hz, 1H), 7.14 (d, J = 3.7 Hz, 1H), 5.65 (s, 1H), 0.19 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 147.7, 141.9, 141.1, 126.7, 125.3, 119.9, 104.4, 91.3, 60.6, -0.1; IR (neat cm^{-1}) 3181, 3017, 2112, 1592, 1494, 1414, 1219, 991, 800; HRMS (DART, M^+ + H) *m/z* 288.0901 (calculated for $C_{15}H_{18}NOSSi$, 288.0878).

1-(5-(3,5-dimethylisoxazol-4-yl)-2-methoxyphenyl)-3-(trimethylsilyl) prop-2-yn-1-ol (10j)



According to the general nucleophilic addition ethynyltrimethyl silane (4.1 mmol, 0.6 mL) in THF (2M, 2.0 mL) and isopropyl magnesium chloride (2M, 4.1 mmol, 2.0 mL) was stirred. At 0 °C was added the aldehyde (2.72 mmol, 0.63 g) in THF (0.1M, 27.2 mL). Following the general workup and flash chromatography (SiO_2, 20 g, 3%MeOH/CH_2Cl_2) alkynol was obtained as a colorless oil (0.86 g, 96%): TLC R_f = 0.4 (3%MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.17 (m, 1H), 6.95 (d, J = 8.2 Hz, 1H), 5.76 (d, J = 5.6 Hz, 1H), 3.90 (s, 3H), 2.38 (s, 3H), 2.24 (s, 3H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 158.7, 156.2, 130.2, 129.2, 128.9, 122.7, 116.1, 111.3, 104.6, 91.0, 60.5, 55.8, 11.5, 10.8, -0.1; IR (neat cm^{-1}) 3038, 2923, 2862, 2724, 1682, 1601, 1245, 1176, 1120, 1014, 825; HRMS (DART, M^+ + H) *m/z* 330.1528 (calculated for $C_{18}H_{24}NO_3Si$, 330.1525).

1-(3,4,5-trimethoxyphenyl)-3-trimethylsilyl)prop-2-yn-1-ol (10k)



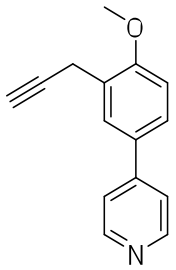
According to the general nucleophilic addition ethynyltrimethyl silane (2.7 mmol, 0.4 mL) in THF (2M, 1.4 mL) and isopropyl magnesium chloride (2M, 2.7 mmol, 1.4 mL) was stirred. At 0 °C was added the aldehyde (1.8 mmol, 0.4 g) in THF (0.1M, 18.0 mL). Following the general workup and flash chromatography (SiO_2, 15 g, 50%EtOAc/Hexane) alkynol was obtained as a brown solid (0.5 g, 95%): TLC R_f = 0.2, 50%EtOAc/Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (s, 2H), 5.33 (d, J = 6.0 Hz, 1H), 3.77(s, 6H), 3.75 (s, 3H), 3.24 (d, J = 6.0 Hz, 1H), 0.14 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 137.6, 136.3, 105.4, 103.9, 91.1, 64.7, 60.7, 56.0, -0.2; IR (neat cm^{-1}) 3426, 2957, 2837, 2169, 1648, 1593, 1460, 1248, 1125, 841; HRMS (DART, $[M\text{-}OH]^+$) *m/z* 277.1285 (calculated for $C_{15}H_{21}O_3Si$, 277.1254).

General Procedure for Propargyl Deoxygenation

To a 10 mL vial flame dried flask was added the TMS- protected alkynol dissolved in anhydrous 0.1M CH_2Cl_2 and cooled to 0 °C. $BF_3{\cdot}OEt_2$ was slowly added followed by Et_3SiH. Equivalence of lewis acid and triethylsilane ratio varies relative to the number of heteroatoms present. After addition, the reaction mixture was brought to room temperature followed by heating to 41 °C and monitored by TLC after working up a small aliquot of the reaction mixture with saturated $NaHCO_3$. *Note*: Although disappearance of the starting alkynol can be observed with few minutes of starting the reaction, it is still proceeding through an intermediate complex which can be found on the baseline in the TLC. The slow disappearance of this complex

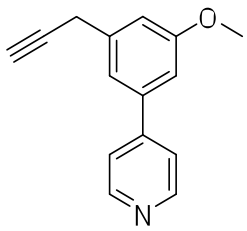
constitute the completion of the reaction and not the starting alkynol. The reaction was quenched with saturated $NaHCO_3$, extracted with EtOAc and dried with the $MgSO_4$. After rotoevaporation, deprotection was carried out by dissolving the TMS-alkyne in 0.2M EtOH and stirring initially for 30min with $AgNO_3$ (3 eq) dissolved in 1.5M water. KCN (10 eq) dissolved in 10M H_2O was added slowly and stirred for 1 h. The reaction mixture was diluted with EtOAc, washed with water and dried with $MgSO_4$. Solvent was evaporated, the crude mixture was pre-absorbed onto silica gel and column chromatography was carried out.

4-(4-methoxy-3-(prop-2-yn-1-yl) phenyl) pyridine (11a)



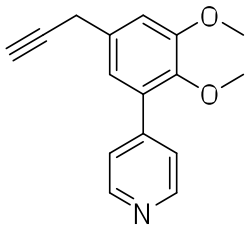
According to general deoxygenation protocol, alkynol (1.0 mmol, 0.3 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (4.0 mmol, 1.3 mL) and triethylsilane (2.0 mmol, 0.3 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 15 g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a white solid (0.17 g, 74%): TLC R_f = 0.3 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, J = 4.3 Hz, 2H), 7.80 (s, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.45 (d, J = 4.9 Hz, 2H), 6.90 (d, J = 8.5 Hz, 1H), 3.85 (s, 3H), 3.60 (s, 2H), 2.21 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 150.3, 148.0, 130.4, 127.6, 126.7, 125.5, 121.2, 110.6, 81.6, 71.2, 55.7, 19.5; IR(neat cm^{-1}) 3164, 2999, 2917, 2834, 2110, 1594, 1508, 1306, 804, 665; HRMS (DART, $M^+ + H$) *m/z* 224.1071 (calculated for $C_{15}H_{14}NO$, 224.1075).

4-(3-methoxy-5-(prop-2-yn-1-yl) phenyl) pyridine (11b)



According to general deoxygenation protocol, alkynol (0.34 mmol, 0.11g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (1.40 mmol, 0.17 mL) and triethylsilane (0.70 mmol, 0.11 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 7 g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a brownish oil (0.05 g, 67%): TLC R_f = 0.3 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.6 Hz, 2H), 7.45 (d, *J* = 5.9 Hz, 2H), 7.18 (s, 1H), 7.00 (s, 1H), 6.96 (s, 1H), 3.84 (s, 3H), 3.63 (d, *J* = 2.4 Hz, 2H), 2.21 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 150.4, 148.2, 140.0, 138.7, 121.9, 119.2, 114.2, 111.4, 81.5, 71.2, 55.6, 25.1; IR(neat cm^{-1}) 3288, 2959, 2931, 2837, 2113, 1592, 1406, 1217, 1049, 816, 627; HRMS (DART, M^+ + H) *m/z* 224.1100 (calculated for $C_{15}H_{14}NO$, 224.1075).

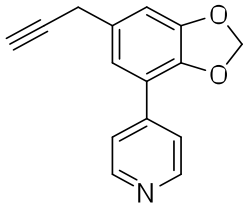
4-(2,3-dimethoxy-5-(prop-2-yn-1-yl) phenyl) pyridine (11c)



According to general deoxygenation protocol, alkynol (1.0 mmol, 0.4 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (5.0 mmol, 1.7 mL) and triethylsilane

(2.5 mmol, 0.4 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 10 g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a yellow brownish solid (0.2 g, 76%): TLC R_f = 0.3 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, J = 6.1, 1.6 Hz, 2H), 7.46 (dd, J = 6.1, 1.6 Hz, 2H), 6.97 (d, J = 1.9 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 3.91 (s, 3H), 3.60 (d, J = 2.7 Hz, 2H), 3.58 (s, 3H), 2.21 (t, J = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 149.6, 146.3, 145.7, 133.0, 132.6, 124.3, 121.3, 112.7, 81.8, 71.1, 61.1, 56.2, 24.9; IR(neat cm^{-1}) 3285, 3034, 2908, 2885, 2836, 2117, 1711, 1404, 1264, 1132, 994, 816, 627; HRMS (DART, M^+ + H) *m/z* 254.1196 (calculated for $C_{16}H_{16}NO_2$, 254.1181).

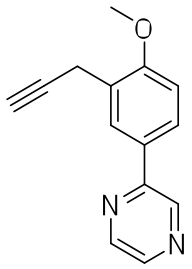
4-(6-(prop-2-yn-1-yl) benzo[d][1,3]dioxol-4-yl)pyridine (11d)



According to general deoxygenation protocol, alkynol (0.75 mmol, 0.24 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (3.70 mmol, 1.20 mL) and triethylsilane (1.90 mmol, 0.30 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 7 g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a pale white solid (0.13 g, 74%): TLC R_f = 0.3 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J = 5.6 Hz, 2H), 7.60 (d, J = 5.9 Hz, 2H), 7.06 (s, 1H), 6.87 (s, 1H), 6.01 (s, 2H), 3.55 (d, J = 2.3 Hz, 2H), 2.20 (t, J = 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 148.8, 144.5, 143.3, 130.8, 122.2, 119.7, 119.5, 109.2, 101.6, 81.8, 71.1, 24.8;

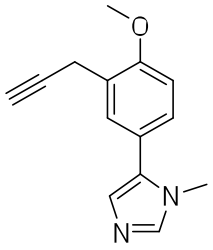
IR(neat cm^{-1}) 3229, 3069, 3031, 2989, 2917, 2114, 1703, 1599, 1407, 1256, 1094, 944, 815, 652; HRMS (DART, $M^+ + H$) *m/z* 238.0883 (calculated for $C_{15}H_{12}NO_2$, 238.0868).

2-(4-methoxy-3-(prop-2-yn-1-yl) phenyl) pyrazine (11e)



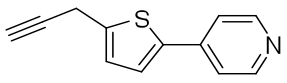
According to general deoxygenation protocol, alkynol (0.9 mmol, 0.3 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3 \cdot OEt_2$ (4.3 mmol, 1.3 mL) and triethylsilane (2.1 mmol, 0.3 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 10 g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a pale yellow solid (0.15 g, 76%): TLC R_f= 0.5 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.56 (s, 1H), 8.42 (s, 1H), 8.17 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.62 (d, *J* = 2.4 Hz, 2H), 2.21 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3, 152.4, 143.9, 142.1, 141.6, 128.7, 127.4, 126.8, 125.2, 110.3, 81.5, 71.1, 55.5, 19.4; IR(neat cm^{-1}) 3201, 3071, 2975, 2933, 2842, 2205, 1607, 1276, 1116, 1018, 809, 697, 433; HRMS (DART, M^+ + H) *m/z* 225.1050 (calculated for $C_{14}H_{13}N_2O$, 225.1028).

5-(4-methoxy-3-(prop-2-yn-1-yl) phenyl)-1-methyl-1H-imidazole (11g)



According to general deoxygenation protocol, alkynol (0.51 mmol, 0.16 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (2.0 mmol, 0.3 mL) and triethylsilane (1.0 mmol, 0.2 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 7 g, 3% MeOH in CH_2Cl_2) deoxygenated alkyne was obtained as a yellow oil (0.08 g, 70%): TLC R_f = 0.1 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 2.1 Hz, 1H), 7.48 (s, 1H), 7.24 – 7.21 (m, 1H), 7.02 (s, 1H), 6.88 (d, J = 8.4 Hz, 1H), 3.85 (s, 3H), 3.61 (s, 3H), 3.58 (d, J = 2.7 Hz, 2H), 2.17 (t, J = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8, 138.8, 133.5, 129.4, 128.5, 127.6, 125.1, 122.2, 110.3, 81.6, 71.1, 55.7, 32.6, 19.4; IR(neat cm^{-1}) 3215, 2969, 2930, 2884, 1658, 1466, 1127, 950, 816, 627; HRMS (DART, $M^+ + H$) *m/z* 227.1204 (calculated for $C_{14}H_{15}N_2O$, 227.1184).

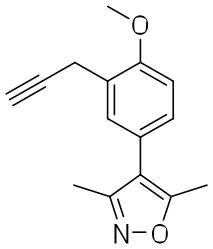
4-(5-(prop-2-yn-1-yl) thiophen-2-yl)pyridine (11i)



According to general deoxygenation protocol, alkynol (0.44 mmol, 0.13 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (1.80 mmol, 0.22 mL) and triethylsilane (0.90 mmol, 0.14 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by HPLC chromatogaraphy with 60% ACN in water; deoxygenated alkyne

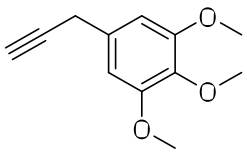
was obtained as a pale white solid (0.06 g, 66%): TLC R_f = 0.4 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.5 Hz, 2H), 7.40 (d, *J* = 5.0 Hz, 2H), 7.33 (d, *J* = 3.6 Hz, 1H), 6.98 (d, *J* = 3.2 Hz, 1H), 3.78 (d, *J* = 2.4 Hz, 2H), 2.24 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 141.5, 141.2, 140.1, 126.8, 125.4, 119.7, 80.5, 71.1, 20.3; IR(neat cm^{-1}) 3181, 3072, 3040, 3017, 2112, 1592, 1414, 1219, 991, 800, 689, 463; HRMS (DART, M^+ + H) *m/z* 200.0556 (calculated for $C_{12}H_{10}NS$, 200.0534).

4-(4-methoxy-3-(prop-2-yn-1-yl) phenyl)-3,5-dimethylisoxazole (11j)



According to general deoxygenation protocol, alkynol (0.33 mmol, 0.11 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (1.70 mmol, 0.21 mL) and triethylsilane (0.80 mmol, 0.13 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 7g, 50% EtOAc in Hexane) deoxygenated alkyne was obtained as a white solid (0.06 g, 74%): TLC R_f = 0.7 (50% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 2.1 Hz, 1H), 7.10 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.59 (d, *J* = 2.5 Hz, 2H), 2.38 (s, 3H), 2.25 (s, 3H), 2.18 (t, *J* = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 159.0, 156.3, 129.8, 128.7, 125.2, 122.7, 116.5, 110.4, 81.7, 71.0, 55.7, 19.4, 11.7, 11.0; IR(neat cm^{-1}) 3243, 3020, 2927, 2838, 2115, 1632, 1504, 1246, 1114, 1027, 815, 684; HRMS (DART, M^+ + H) *m/z* 242.1195 (calculated for $C_{15}H_{16}NO_2$, 242.1181).

1,2,3 trimethoxy-5- (prop-2-yn-1-yl)benzene (11k)



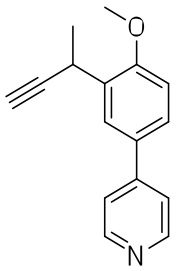
According to general deoxygenation protocol, alkynol (0.33 mmol, 0.10 g) dissolved in 0.1M CH_2Cl_2 was subjected to deoxygenation with $BF_3{\cdot}OEt_2$ (1.32 mmol, 0.16 mL) and triethylsilane (0.66 mmol, 0.22 mL) at 41 °C. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 7g, 15% EtOAc in Hexane) deoxygenated alkyne was obtained as a colorless oil (0.03 g, 45%): TLC R_f = 0.5 (25% EtOAc in Hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 2H), 3.85 (s, 6H), 3.81 (s, 3H), 3.54 (d, J = 2.6 Hz, 2H), 2.18 (t, J = 2.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 136.8, 131.7, 104.9, 81.9, 70.6, 60.9, 56.1, 29.7, 25.1; IR(neat cm^{-1}) 3284, 2938, 2837, 2118, 1590, 1504, 1233, 1122, 1004, 814; HRMS (DART, $M^+ + H$) *m/z* 207.1059 (calculated for $C_{12}H_{15}O_3$, 207.1021).

General Procedure for Propargyl Methylation

To a 100 mL flame dried flask under argon was added CH_2Cl_2 (1M) at room temperature and cooled to 0 °C. $TiCl_4$ (1M in toluene, 1 eq) was added followed by dimethyl zinc (1.2M in toluene, 2 eq) and stirred at 0 °C for 30 minutes. To the yellow heterogeneous mixture, alkynol (1 eq) dissolved in 0.1M CH_2Cl_2 was added dropwise for 10 min. TLC was performed on a small aliquot quenched with MeOH. After ~1 h, the reaction was stopped by a slow dropwise addition of MeOH. Care should be taken to avoid frothing and addition of MeOH continued until the reaction turns into a homogeneous yellow solution. The crude mixture was stirred at room temperature for 5 minutes and pushed through a plug of silica gel. Solvent was evaporated and

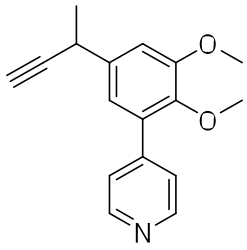
deprotection was carried out by dissolving the TMS-alkyne in 0.2M EtOH and stirring initially for 30min with $AgNO_3$ (3 eq) dissolved in 1.5M water. KCN (10 eq) dissolved in 10M H_2O was added slowly and stirred for 1h. The reaction mixture was diluted with EtOAc, washed with water and dried with $MgSO_4$. Solvent was evaporated, the crude mixture was pre-absorbed onto silica gel and column chromatography was carried out with 3% MeOH in CH_2Cl_2.

4-(3-(but-3-yn-2-yl)-4-methoxyphenyl) pyridine (12a)



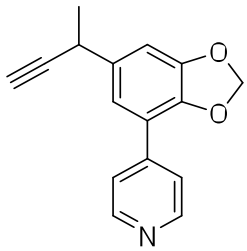
According to the general methylation protocol, alkynol (0.33 mmol, 0.10 g) in CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (0.33 mmol, 0.33 mL) and dimethylzinc (0.66 mmol, 0.50 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 5g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a yellow solid (51.6 mg, 66%): TLC R_f = 0.2 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, J = 5.1 Hz, 2H), 7.87 (d, J = 2.2 Hz, 1H), 7.63 – 7.32 (m, 3H), 6.93 (d, J = 8.5 Hz, 1H), 4.21 (qd, J = 7.1, 2.4 Hz, 1H), 3.87 (s, 3H), 2.25 (d, J = 2.4 Hz, 1H), 1.46 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.2, 150.2, 148.2, 132.0, 130.5, 126.7, 126.6, 121.4, 111.1, 87.3, 70.2, 55.8, 25.7, 22.9; IR (neat cm^{-1}) 3222, 3075, 2980, 2108, 1594, 1484, 1255, 803; HRMS (DART, $M^+ + H$) *m/z* 238.1256 (calculated for $C_{16}H_{16}NO$, 238.1232).

4-(5-(but-3-yn-2-yl)-2,3-dimethoxyphenyl) pyridine (12c)



According to the general methylation protocol, alkynol (0.6 mmol, 0.2 mg) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (0.6 mmol, 0.6 mL) and dimethylzinc (1.2 mmol, 1.0 mL) in 0.1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 15 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a yellow oil (0.16 g, 65%): TLC R_f = 0.2 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (br s, 2H), 7.45 (d, J = 4.1 Hz, 2H), 7.00 (s, 1H), 6.92 (s, 1H), 3.90 (s, 3H), 3.74 (q, J = 6.7 Hz, 1H), 3.57 (s, 3H), 2.27 (s, 1H), 1.50 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 149.8, 146.2, 145.6, 139.1, 133.0, 124.2, 120.2, 111.7, 86.9, 70.8, 61.0, 56.2, 31.7, 24.4; IR(neat cm^{-1}) 3299, 3050, 2975, 2933, 2873, 2837, 2003.75, 1586, 1406, 1264, 1139, 734; HRMS (DART, M^+ + H) *m/z* 268.1336 (calculated for $C_{17}H_{18}NO_2$, 268.1338).

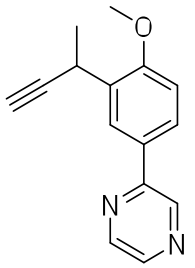
4-(6-(but-3-yn-2-yl) benzo[d][1,3]dioxol-4-yl) pyridine (12d)



According to the general methylation protocol, alkynol (6.3 mmol, 2.0 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (6.3 mmol, 6.3 mL)and dimethylzinc (12.6 mmol, 10.5

mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 20 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a yellow oil (1.0 g, 62%): TLC R_f = 0.2 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J* = 5.4 Hz, 2H), 7.62 (dd, *J* = 6.0, 1.4 Hz, 2H), 7.11 (d, *J* = 1.4 Hz, 1H), 6.93 (d, *J* = 1.5 Hz, 1H), 6.03 (d, *J* = 1.5 Hz, 2H), 3.73 (qd, *J* = 7.1, 2.4 Hz, 1H), 2.28 (d, *J* = 2.5 Hz, 1H), 1.50 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 148.8, 144.5, 143.5, 137.6, 122.3, 119.5, 118.8, 108.2, 101.6, 86.9, 70.8, 31.7, 24.6; IR(neat cm^{-1}) 3200, 3026, 2929, 2786, 2106, 1737, 1596, 1402, 1197, 1040, 938, 823, 623; HRMS (DART, M^+ + H) *m/z* 257.1055 (calculated for $C_{16}H_{14}NO_2$, 257.1025).

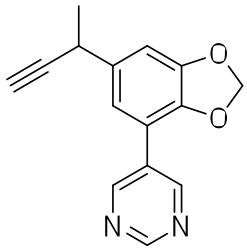
2-(3-(but-3-yn-2-yl)-4-methoxyphenyl) pyrazine (12e)



According to the general methylation protocol, alkynol (0.5 mmol, 0.2 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (0.5 mmol, 0.5 mL) and dimethylzinc (1.0 mmol, 0.9 mL) in 0.1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 10 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a pale yellow solid (0.12 g, 60%): TLC R_f = 0.5 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (br s, 1H), 8.53 (br s, 1H), 8.38 (br s, 1H), 8.22 (d, *J* = 2.3 Hz, 1H), 7.86 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 4.18 (qd, *J* = 7.0, 2.5 Hz, 1H), 3.83 (s, 3H), 2.25 (d, *J* = 2.5 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7,

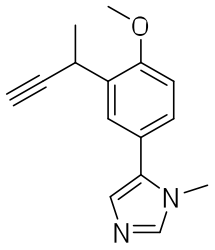
152.7, 144.1, 142.1, 141.8, 131.8, 128.9, 126.8, 126.5, 110.9, 87.1, 70.1, 55.7, 25.6, 22.6; IR(neat cm^{-1}) 3182, 3055, 2973, 2875, 2101, 1605, 1248, 1126, 1013, 812, 713; HRMS (DART, $M^+ + H$) *m/z* 239.1212 (calculated for $C_{15}H_{15}NO_2$, 239.1184).

5-(6-(but-3-yn-2-yl) benzo[d][1,3]dioxol-4-yl) pyrimidine (12f)



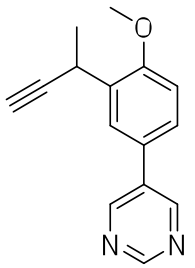
According to the general methylation protocol, alkynol (1.0 mmol, 0.3 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (1.0 mmol, 1 mL) and dimethylzinc (2.0 mmol, 1.6 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 15 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a pale white solid (0.14 g, 60%): TLC R_f = 0.3 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1H), 9.02 (s, 2H), 7.02 (d, *J* = 1.4 Hz, 1H), 6.90 (d, *J* = 1.4 Hz, 1H), 6.00 (s, 2H), 3.70 (qd, *J* = 7.1, 2.4 Hz, 1H), 2.27 (d, *J* = 2.4 Hz, 1H), 1.46 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 155.4, 148.7, 144.2, 137.9, 129.8, 118.2, 115.4, 108.2, 101.7, 86.6, 70.9, 31.5, 24.4; IR(neat cm^{-1}) 3200, 2910, 2877, 2787, 1726, 1494, 1407, 1349, 1262, 1176, 1045, 940, 855, 718; HRMS (DART, $M^+ + H$) *m/z* 253.0968 (calculated for $C_{15}H_{13}N_2O_2$, 253.0977).

5-(3-(but-3-yn-2-yl)-4-methoxyphenyl)-1-methyl-1H-imidazole (12g)



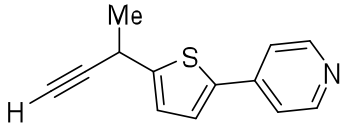
According to the general methylation protocol, alkynol (1.11 mmol, 0.35 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (1.11 mmol, 1.10 mL) and dimethylzinc (2.22 mmol, 1.90 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 15 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a yellow oil (0.17 g, 62%): TLC R_f = 0.1 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.45 (s, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.02 (s, 1H), 6.87 (d, J = 8.3 Hz, 1H), 4.16 (q, J = 6.3 Hz, 1H), 3.83 (s, 3H), 3.60 (s, 3H), 2.18 (s, 1H), 1.42 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 138.8, 133.5, 131.5, 128.3, 128.2, 127.6, 122.3, 110.7, 87.3, 70.0, 55.7, 32.5, 25.6, 22.8; IR(neat cm^{-1}) 3283, 2973, 2931, 2837, 1612, 1490, 1249, 1024, 813, 650; HRMS (DART, M^+ + H) *m/z* 241.1362 (calculated for $C_{15}H_{17}N_2O$, 241.1341).

5-(3-(but-3-yn-2-yl)-4-methoxyphenyl) pyrimidine (12h)



According to the general methylation protocol, alkynol (0.97 mmol, 0.31 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (0.97 mmol, 0.97 mL)and dimethylzinc (1.94 mmol, 1.62 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 10 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a white solid (0.14 g, 56%): TLC R_f = 0.2 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.91 (s, 2H), 7.79 (d, *J* = 2.3 Hz, 1H), 7.42 (dd, *J* = 8.4, 2.3, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 4.20 (qd, *J* = 7.0, 2.4 Hz, 1H), 3.88 (s, 3H), 2.24 (d, *J* = 2.5 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 157.0, 154.6, 134.2, 132.4, 126.7, 126.6, 126.5, 111.4, 87.0, 70.4, 55.8, 25.7, 22.8; IR (neat cm^{-1}) 3265, 3046, 2832, 1889, 1605, 1252, 724. HRMS (DART, M^+ + H) *m/z* 239.1207 (calculated for $C_{15}H_{15}N_2O$, 239.1184).

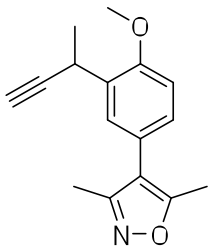
4-[5-(1-Methyl-prop-2-ynyl)-thiophen-2-yl]-pyridine (12i)



According to the general methylation protocol, alkynol (0.52 mmol, 0.15 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (0.52 mmol, 1.0 mL) and dimethylzinc (1.04 mmol, 1.60 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 5 g, 1:1 EtoAc/hexane) methylated alkyne was obtained as a yellow solid (0.17 g, 65%): TLC R_f = 0.8 (1:1 EtoAc/hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.6 Hz, 2H), 7.48 – 7.41 (m, 2H), 7.35 (d, *J* = 3.7 Hz, 1H), 7.03 (dd, *J* = 3.6, 1.0 Hz, 1H), 4.06 (qd, *J* = 6.9, 2.1 Hz, 1H), 2.36 (d, *J* = 2.5 Hz, 1H), 1.65 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 148.5, 141.4, 139.5, 125.3, 125.0, 119.5, 85.6, 70.5, 27.4, 24.0; IR

(neat cm^{-1}) 3198, 2984, 2934, 1594, 1460, 1414, 1220, 991, 802, 690, 525; HRMS (DART, M^+ + H) *m/z* 214.0705 (calculated for $C_{13}H_{12}NS$, 214.0690).

4-(3-(but-3-yn-2-yl)-4-methoxyphenyl)-3,5-dimethylisoxazole (12j)

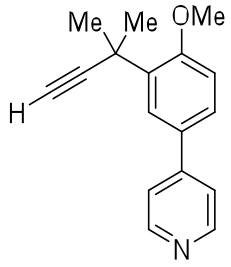


According to the general methylation protocol, alkynol (1.0 mmol, 0.32 g) in 0.1M CH_2Cl_2 was added to the pre-mixed solution of $TiCl_4$ (1.0 mmol, 1.0 mL) and dimethylzinc (2.0 mmol, 1.6 mL) in 1M CH_2Cl_2. Following the general workup and deprotection, the crude mixture was purified by flash chromatography (SiO_2, 20 g, 3% MeOH in CH_2Cl_2) methylated alkyne was obtained as a colorless oil (0.17 g, 65%): TLC R_f = 0.8 (3% MeOH in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 4.19 (q, *J* = 6.8 Hz, 1H), 3.85 (s, 3H), 2.38 (s, 3H), 2.25 (s, 3H), 2.20 (s, 1H), 1.44 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 159.0, 155.5, 131.6, 128.8, 128.6, 122.9, 116.5, 110.8, 87.4, 69.9, 55.7, 25.6, 22.9, 11.7, 11.0; IR(neat cm^{-1}) 3292, 2973, 2931, 2837, 2125, 1606, 1505, 1246, 1130, 1026, 637; HRMS (DART, M^+ + H) *m/z* 256.1361 (calculated for $C_{16}H_{18}NO_2$, 256.1338).

Tertiary propargyl alcohol formation from secondary propargyl alcohol. Secondary propargyl was added in dichloromethane to a dried round bottom flask fitted with a stir bar and dried MnO_2 (20 equiv). Once complete by TLC, reaction mixture filtered through celite and dried in vacuo. Residue brought up in THF, placed under argon, and methyl magnesium bromide (3.0 M in Et_2O, 1.5 equiv) added via syringe. Once complete by TLC, saturated ammonium

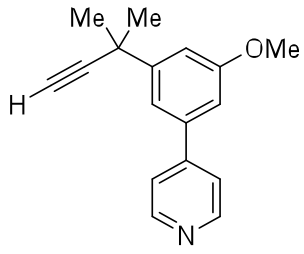
chloride was added. The product was extracted 3x with EtOAc, washed with brine, dried over sodium sulfate, filtered, and dried in vacuo. The tertiary alcohol product was used with no further purification.

4-[3-(1,1-Dimethyl-prop-2-ynyl)-4-methoxy-phenyl]-pyridine (13a)



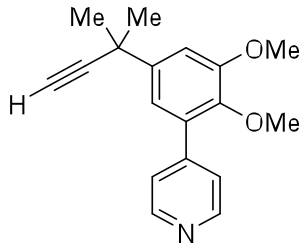
The tertiary alcohol (0.15 g, 0.461 mmol) was subjected to the general procedure for methylation. Once completed, dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a white solid (0.08 g, 45%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 2H), 8.07 (s, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.02 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H), 2.47 (s, 1H), 1.77 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 150.3, 148.3, 133.9, 130.1, 126.8, 121.4, 112.5, 91.4, 70.4, 55.6, 36.1, 29.0; IR (neat cm^{-1}) 3295, 2972, 2934, 1597, 1487, 1283, 1253, 1221, 1081, 1024, 808, 637; HRMS (DART, M^+ + H) *m/z* 252.1326 (calculated for $C_{17}H_{18}NO$, 252.1368).

4-[3-(1,1-Dimethyl-prop-2-ynyl)-5-methoxy-phenyl]-pyridine (13b)



The tertiary alcohol (0.150 g, 0.461 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a white solid (0.08 g, 46%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 – 8.54 (m, 2H), 7.63 – 7.48 (m, 2H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.03 (d, *J* = 1.9 Hz, 1H), 3.91 (s, 3H), 2.42 (s, 1H), 1.67 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 150.4, 149.1, 148.7, 139.8, 122.0, 117.1, 112.7, 110.6, 90.7, 70.5, 55.6, 36.2, 31.7; IR (neat cm^{-1}) 3288, 2974, 2932, 1592, 1549, 1451, 1405, 1322, 1264, 1049, 818, 642; HRMS (DART, M^+ + H) *m/z* 252.1407 (calculated for $C_{17}H_{18}NO$, 252.1368).

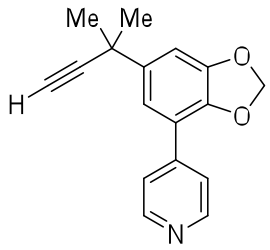
4-[5-(1,1-Dimethyl-prop-2-ynyl)-2,3-dimethoxy-phenyl]-pyridine (13c)



The tertiary alcohol (0.150 g, 0.422 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a yellow solid (0.08 g, 47%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 2H), 7.52 (d, *J* = 4.2 Hz, 2H), 7.24 (d, *J* = 1.7 Hz, 1H), 7.12 (d, *J* = 1.8 Hz, 1H), 3.96 (s, 3H), 3.64 (s, 3H), 2.40 (s, 1H), 1.65 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 149.7, 146.5, 145.4, 142.9, 132.6, 124.4, 118.9, 111.1, 90.8, 70.3, 61.0, 56.2, 36.0, 31.8; IR (neat cm^{-1}) 3286, 2973, 2933, 1594, 1547, 1481, 1462, 1405, 1278,

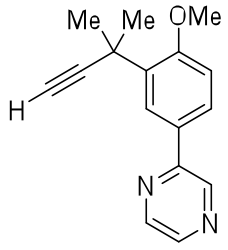
1240, 1146, 1042, 1005, 827, 645; HRMS (DART, M^+ + H) *m/z* 282.1504 (calculated for $C_{18}H_{20}NO_2$, 282.1494).

4-[6-(1,1-Dimethyl-prop-2-ynyl)-benzo[1,3] dioxol-4-yl]-pyridine (13d)



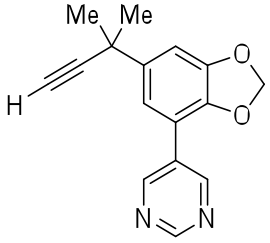
The tertiary alcohol (0.150 g, 0.442 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as an off-white solid (0.07 g, 43%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 2H), 7.69 (d, *J* = 5.2 Hz, 2H), 7.42 – 7.31 (m, 1H), 7.12 (d, *J* = 1.8 Hz, 1H), 6.08 (s, 2H), 2.42 (s, 1H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 148.6, 144.2, 143.6, 141.4, 122.4, 119.0, 117.6, 107.3, 101.6, 90.8, 70.4, 70.4, 35.9, 31.9; IR (neat cm^{-1}) 3291, 3030, 2928, 1969, 1597, 1544, 1474, 1403, 1221, 1043, 943, 823, 651; HRMS (DART, M^+ + H) *m/z* 266.1208 (calculated for $C_{17}H_{16}NO_2$, 266.1181).

2-[3-(1,1-Dimethyl-prop-2-ynyl)-4-methoxy-phenyl]-pyrazine (13e)



The tertiary alcohol (0.150 g, 0.459 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a white solid (0.08 g, 46%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.62 (s, 1H), 8.47 (s, 1H), 8.42 (d, *J* = 2.0 Hz, 1H), 7.95 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 1H), 3.96 (s, 3H), 2.46 (s, 1H), 1.78 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 153.1, 144.2, 142.2, 134.0, 128.6, 127.1, 126.7, 112.4, 91.4, 70.2, 55.6, 36.0, 29.1; IR (neat cm^{-1}) 3292, 2971, 2932, 1605, 1503, 1427, 1279, 1252, 1143, 1078, 1025, 816, 634; HRMS (DART, M^+ + H) *m/z* 253.1322 (calculated for $C_{16}H_{17}N_2O$, 253.1341).

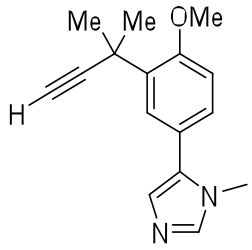
5-[6-(1,1-Dimethyl-prop-2-ynyl)-benzo[1,3] dioxol-4-yl]-pyrimidine (13f)



The tertiary alcohol (150 mg, 0.441 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a yellow solid (0.08 g, 42%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.20 (s, 1H), 9.12 (s, 2H), 7.32 (d, *J* = 1.8 Hz, 1H), 7.13 (d, *J* = 1.8 Hz, 1H), 6.09 (s, 2H), 2.42 (s, 1H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 155.4, 148.5, 143.9, 141.7, 130.0, 117.0, 114.9, 107.1, 101.6, 90.4, 70.4, 35.8, 31.7; IR (neat cm^{-}

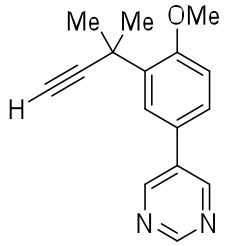
[1]) 3295, 2977, 2167, 1551, 1408, 1262, 1178, 1038, 940, 855, 724, 632; HRMS (DART, $M^+ + H$) *m/z* 267.1109 (calculated for $C_{16}H_{15}N_2O_2$, 267.1133).

5-[3-(1,1-Dimethyl-prop-2-ynyl)-4-methoxy-phenyl]-1-methyl-1H-imidazole (13g)



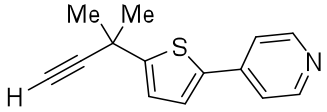
The tertiary alcohol (150 mg, 0.457 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a yellow solid (0.07 g, 44%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.2 Hz, 1H), 7.53 (s, 1H), 7.29 (dd, *J* = 8.3, 2.3 Hz, 2H), 7.08 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 3.92 (s, 3H), 3.68 (s, 3H), 2.42 (s, 1H), 1.74 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 138.7, 133.5, 133.3, 128.3, 128.3, 127.8, 127.5, 121.8, 112.0, 91.4, 70.1, 55.4, 35.9, 32.5, 28.8; IR (neat cm^{-1}) 3288, 2927, 2853, 1767, 1713, 1492, 1366, 1252, 1196, 1080, 1024, 817, 637; HRMS (DART, $M^+ + H$) *m/z* 255.1523 (calculated for $C_{16}H_{19}N_2O$, 255.1497).

5-[3-(1,1-Dimethyl-prop-2-ynyl)-4-methoxy-phenyl]-pyrimidine (13h)



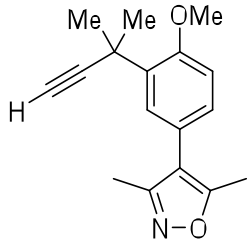
The tertiary alcohol (0.15 g, 0.459 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a white solid (0.07 g, 43%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 – 9.16 (m, 1H), 9.01 (s, 2H), 8.00 (d, *J* = 2.3 Hz, 1H), 7.49 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 3.95 (s, 3H), 2.47 (s, 1H), 1.77 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 156.9, 154.6, 134.4, 126.9, 126.8, 126.3, 112.8, 91.3, 70.7, 70.7, 55.6, 36.2, 29.0; IR (neat cm^{-1}) 3290, 2970, 2931, 1606, 1550, 1500, 1389, 1358, 1286, 1252, 1223, 1080, 1022, 895, 815, 726, 627; HRMS (DART, M^+ + H) *m/z* 253.1316 (calculated for $C_{16}H_{17}N_2O$, 253.1341).

4-[5-(1,1-Dimethyl-prop-2-ynyl)-thiophen-2-yl]-pyridine (13i)



The tertiary alcohol (0.150 g, 0.498 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a yellow solid (0.07 g, 40%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (s, 2H), 7.46 (d, *J* = 5.1 Hz, 2H), 7.35 (d, *J* = 3.8 Hz, 1H), 7.07 (d, *J* = 3.8 Hz, 1H), 2.41 (s, 1H), 1.73 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 150.3, 141.5, 139.1, 124.9, 124.3, 119.6, 89.5, 69.7, 34.0, 32.4; IR (neat cm^{-1}) 3284, 2987, 2967, 1594, 1495, 1412, 1221, 991, 808, 652; HRMS (DART, M^+ + H) *m/z* 228.0867 (calculated for $C_{14}H_{14}NS$, 228.0847).

4-[3-(1,1-Dimethyl-prop-2-ynyl)-4-methoxy-phenyl]-3,5-dimethyl-isoxazole (13j)



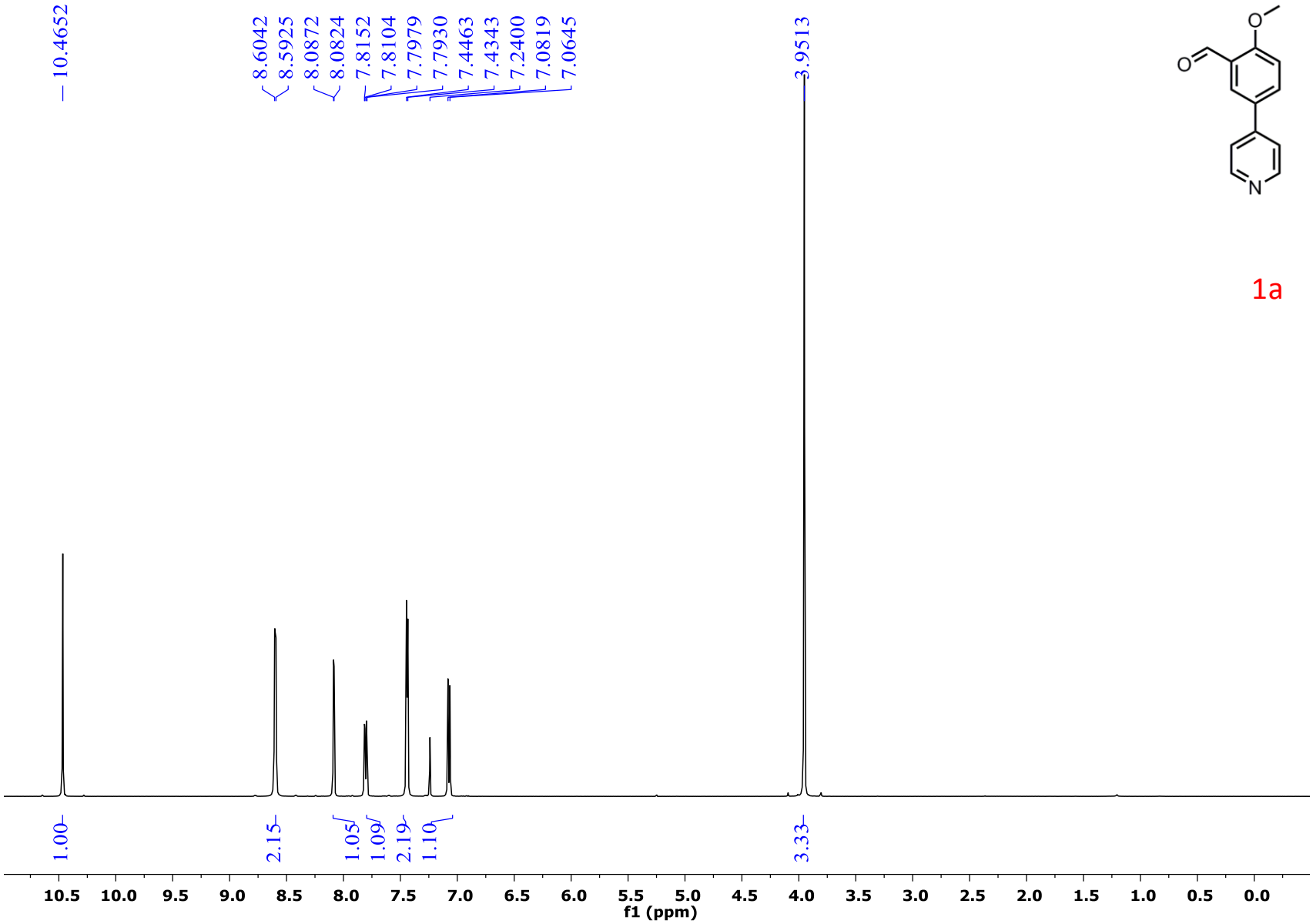
The tertiary alcohol (150 mg, 0.437 mmol) was subjected to the general procedure for methylation. Dried residue isolated from silica plug dissolved in MeOH and K_2CO_3 (2 equiv) added. Stirred until complete by TLC. The title compound was purified via column chromatography (silica gel, 1:1 ethyl acetate/hexanes) and isolated as a yellow solid (0.08 g, 47%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 2.2 Hz, 1H), 7.15 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 3.92 (s, 3H), 2.44 (s, 3H), 2.42 (s, 1H), 2.31 (s, 3H), 1.74 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 158.9, 157.0, 133.4, 128.7, 128.4, 122.3, 116.4, 112.1, 91.4, 70.0, 55.3, 35.9, 28.9, 11.6, 10.9; IR (neat cm^{-1}) 3288, 2970, 2930, 1603, 1505, 1453, 1358, 1251, 1218, 1080, 1026, 819, 642; HRMS (DART, M^+ + H) *m/z* 270.1477 (calculated for $C_{17}H_{20}NO_2$, 270.1494).

References

(1) Bolstad, D.B.; Bolstad, E.S.D.; Frey, K.M; Wright, D.L.; Anderson, A.C. *J. Med. Chem*, **2008**, *51*, 6839-6852

(2) Wielens, J.; Headey, S.J.; Deadman, J.J.; Phodes, D.I.; Parker, M.W.; Chalmers, D.K.; Scanlon, M.J. *ChemMedChem* **2011**, *6*, 258-261

(3) Tadross, P.M.; Gilmore, C.D.; Bugga, P.; Virgil, S.C.; Stoltz, B.M. *Org. Lett.* **2010**, *12*, 1224-1227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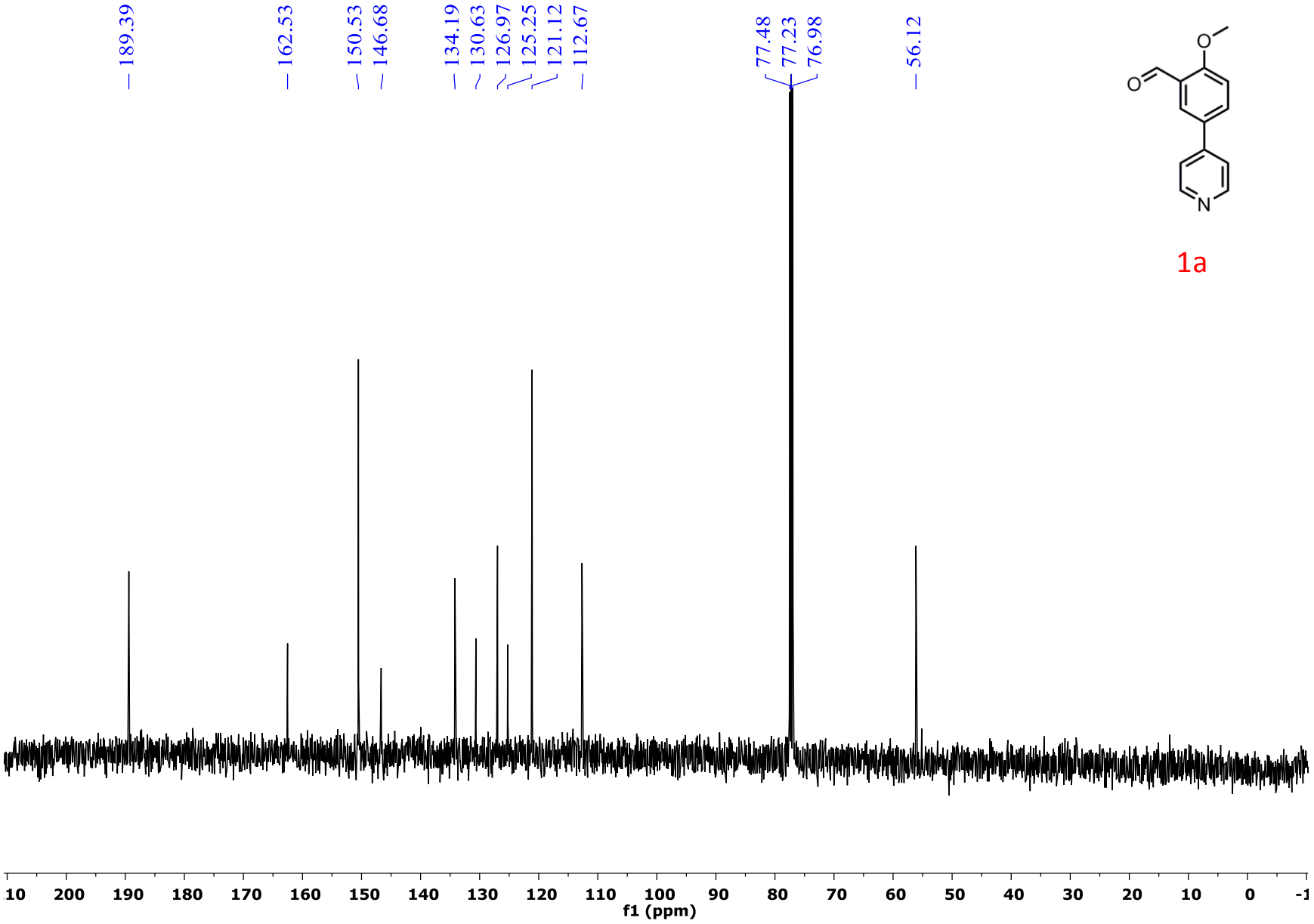
7.4343
7.2400
7.0819
7.0645
3.9513
O
O
N
1a
1.00
2.15
1.05
1.09
2.19
1.10
3.33
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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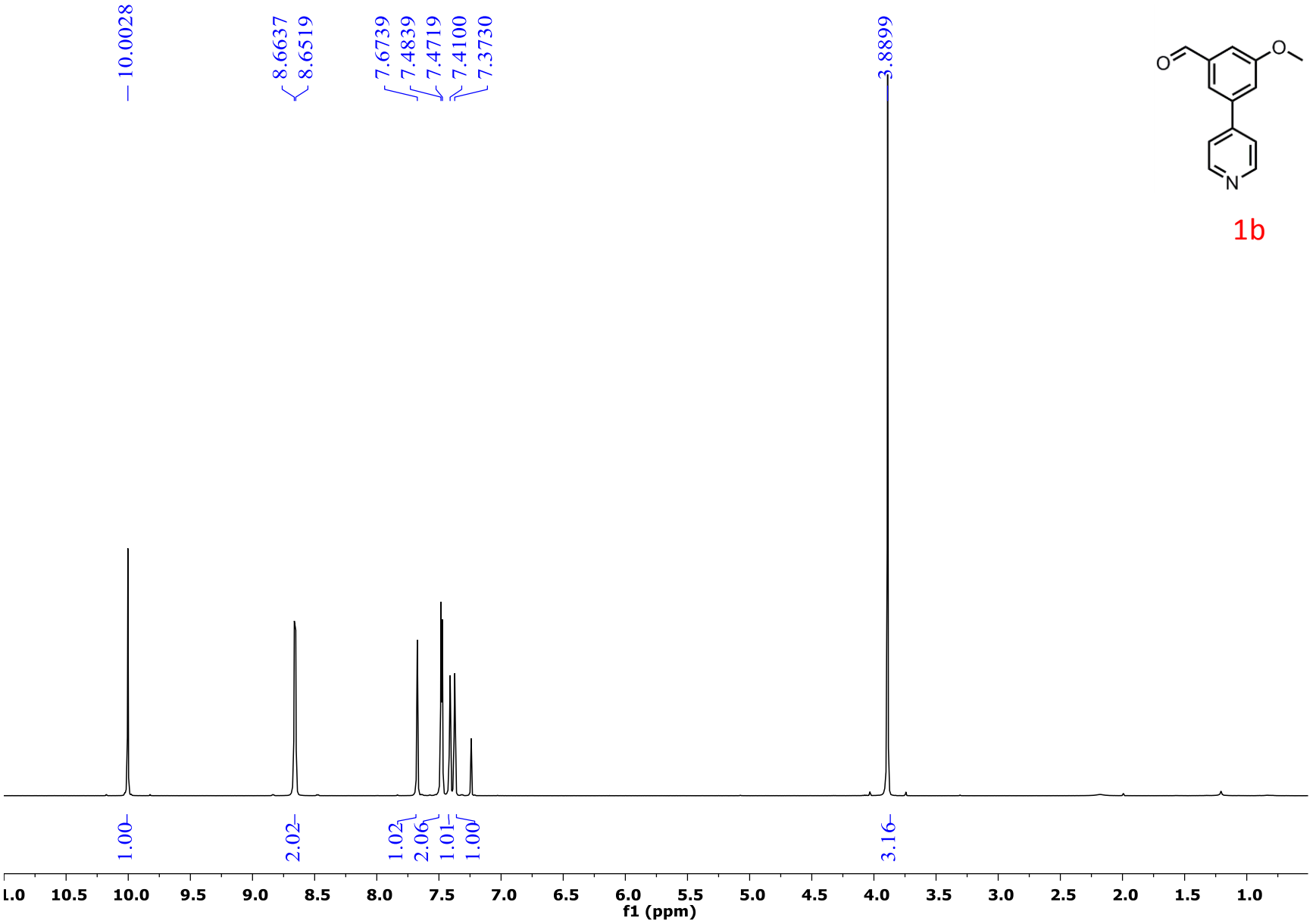
1a
f1 (ppm)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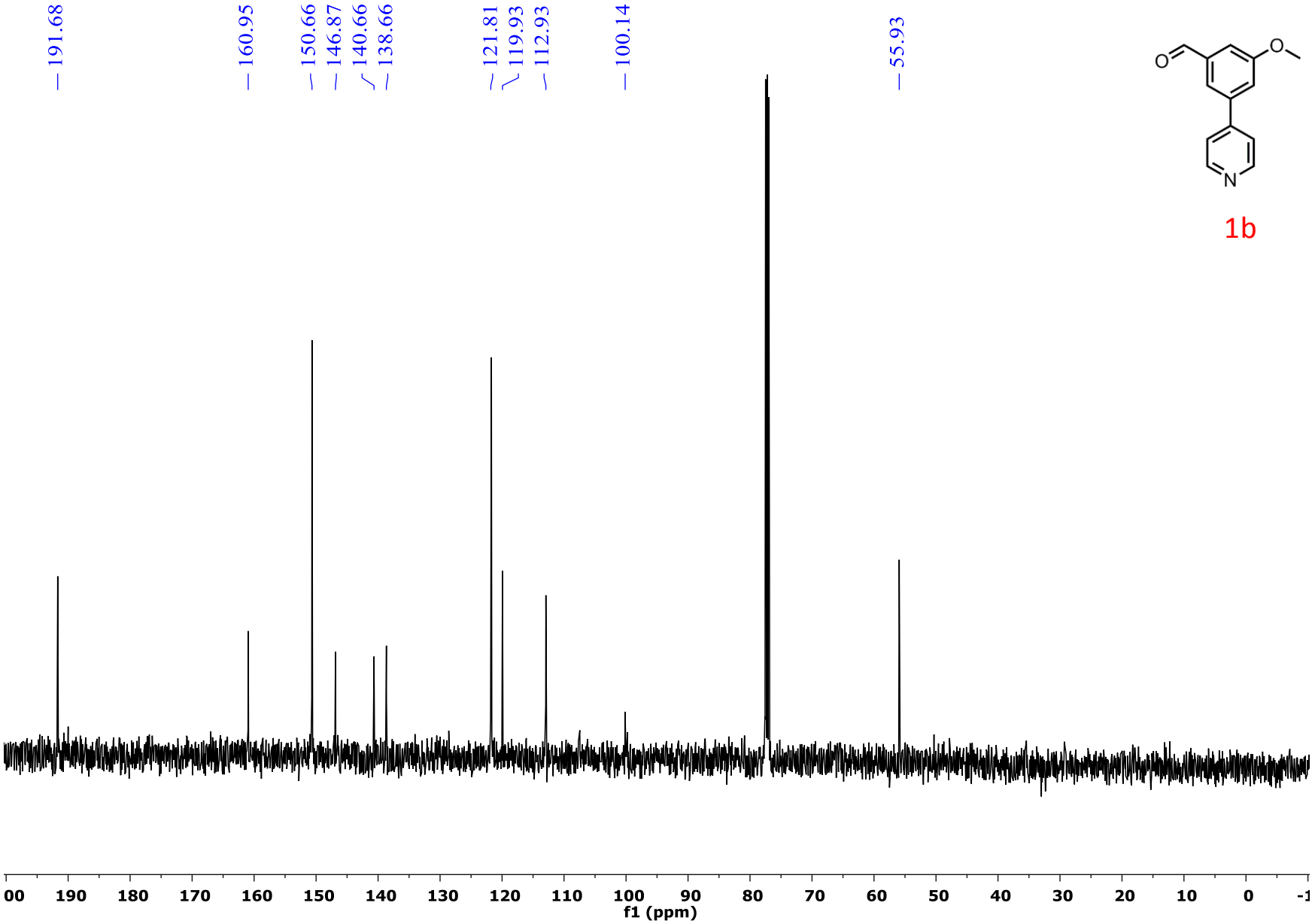
1b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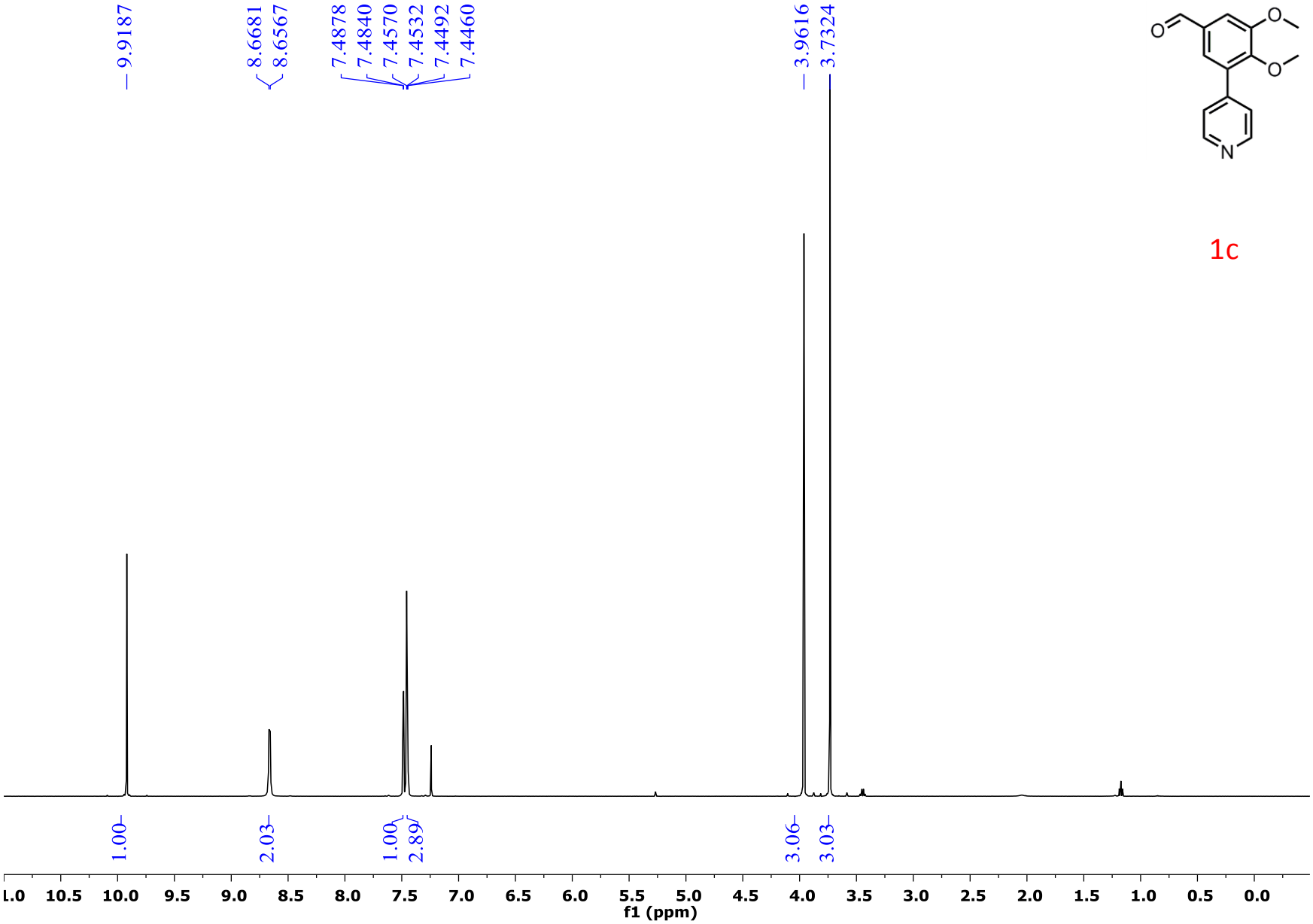
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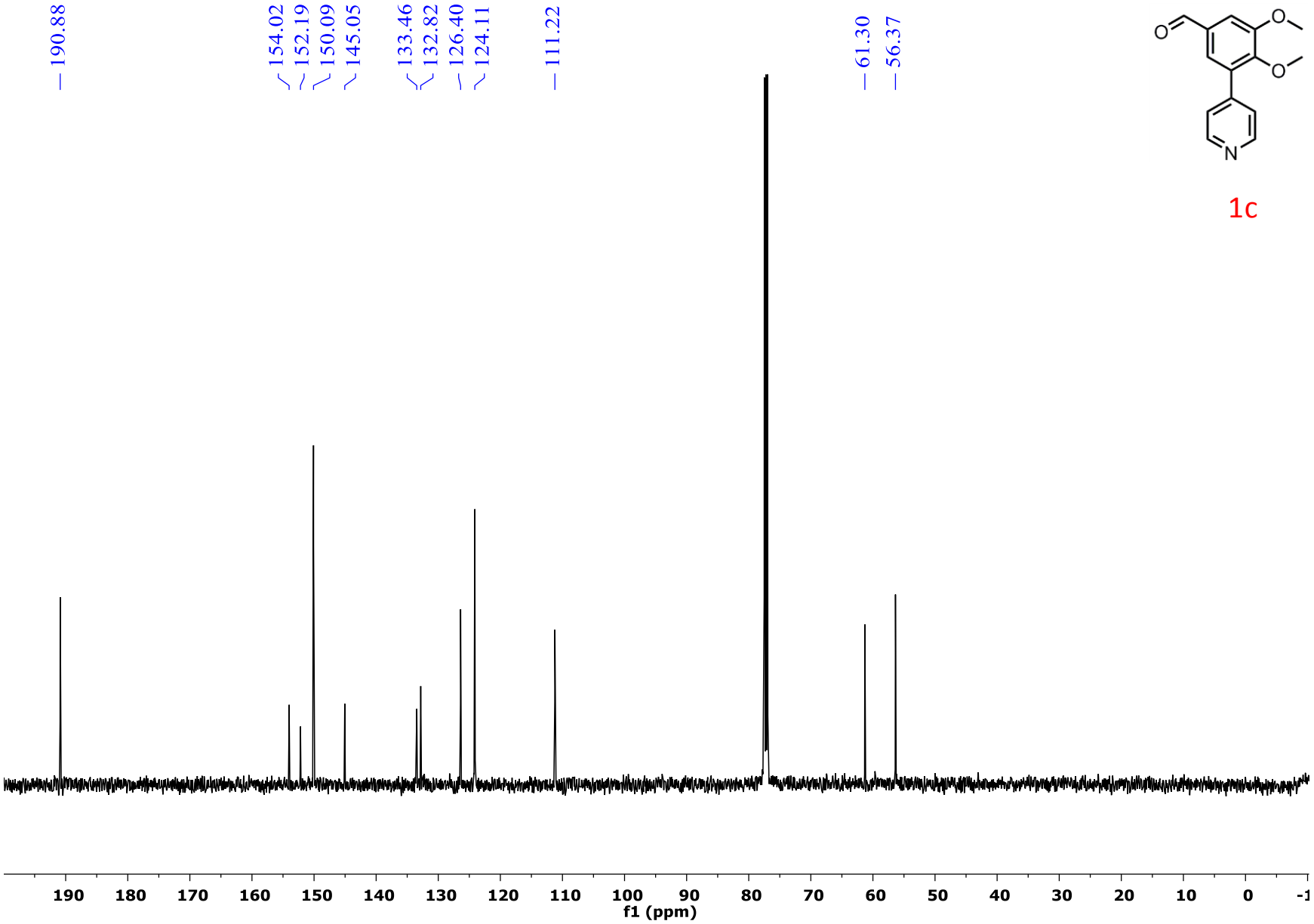
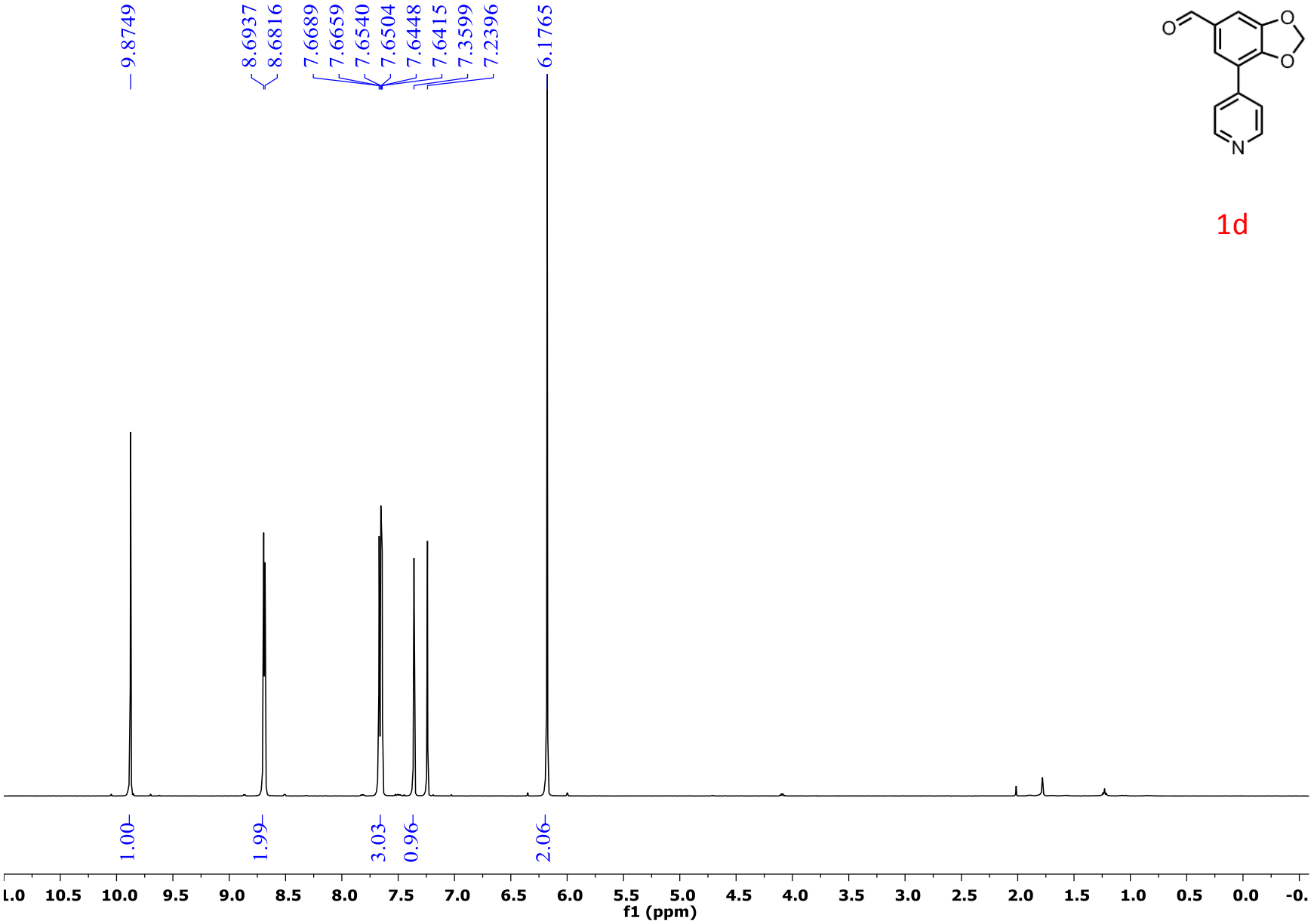
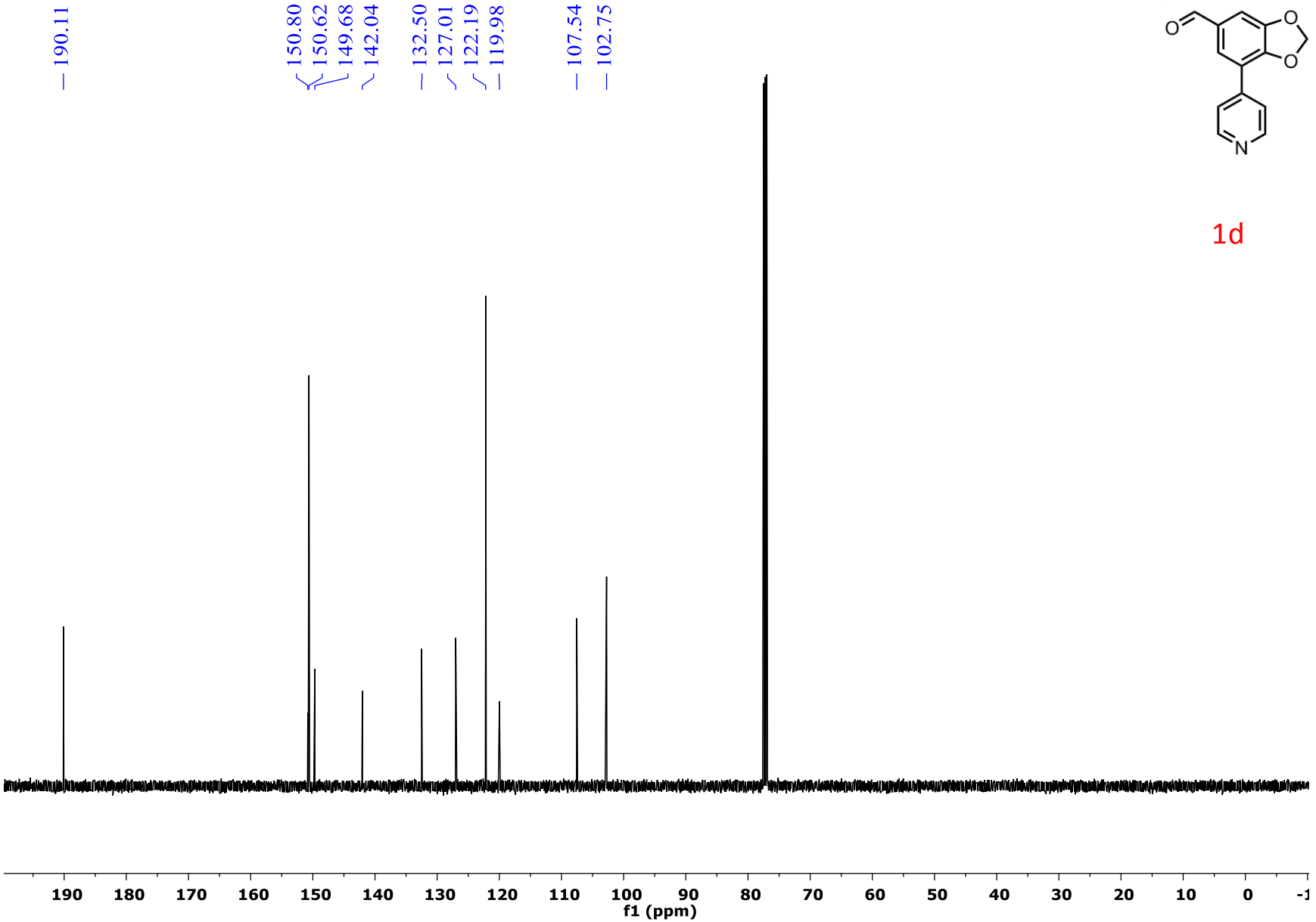
3.03
f1 (ppm)

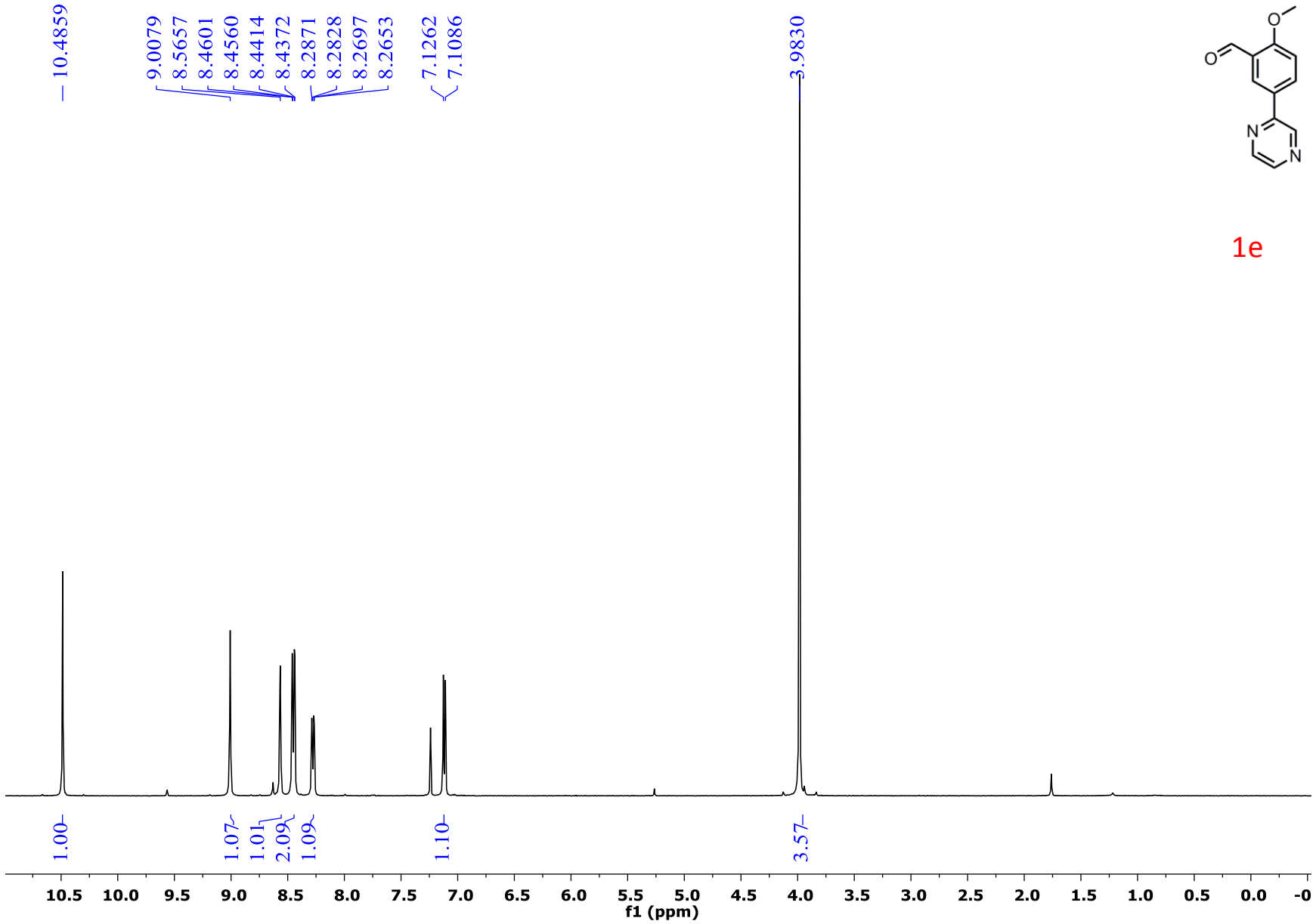
1c


190.88
154.02
152.19
150.09
145.05
133.46
132.82
126.40
124.11
111.22
61.30
56.37
O
O
O
N
1c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

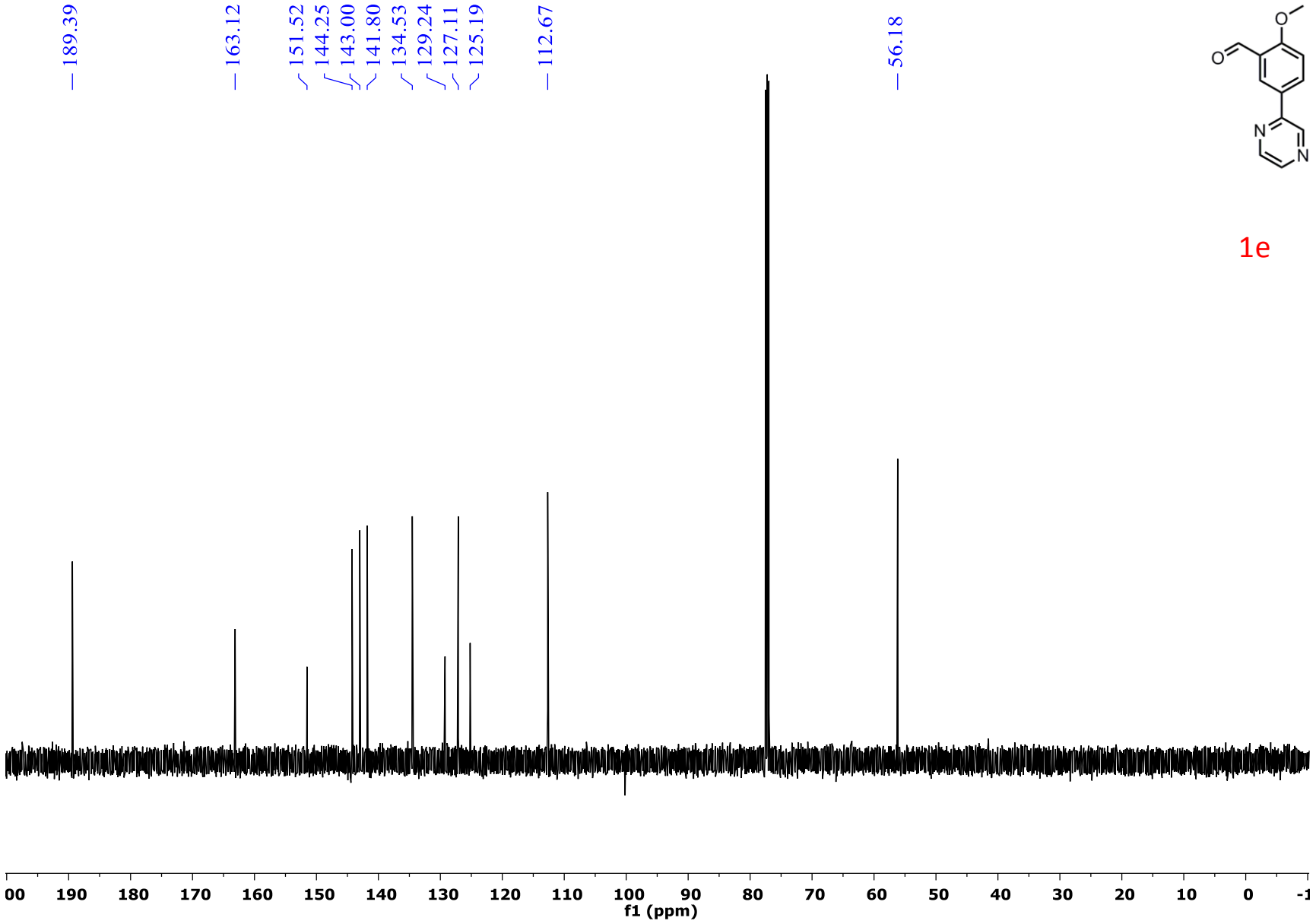

9.8749
8.6937
8.6816
7.6689
7.6659
7.6540
7.6504
7.6448
7.6415
7.3599
7.2396
6.1765
1.00
1.99
3.03
0.96
2.06
f1 (ppm)

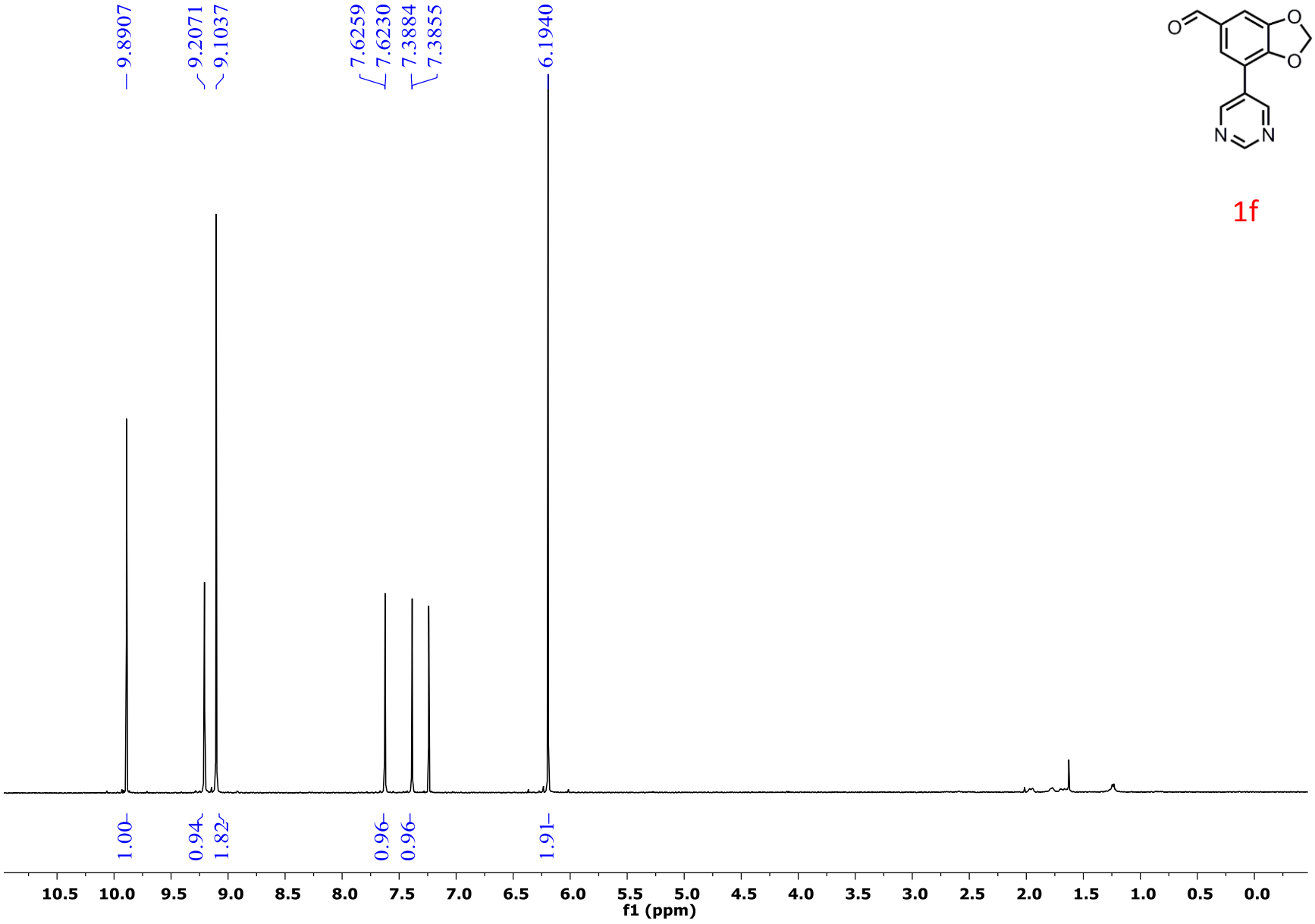
1d


190.11
150.80
150.62
149.68
142.04
132.50
127.01
122.19
119.98
107.54
102.75
O
O
O
N
1d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

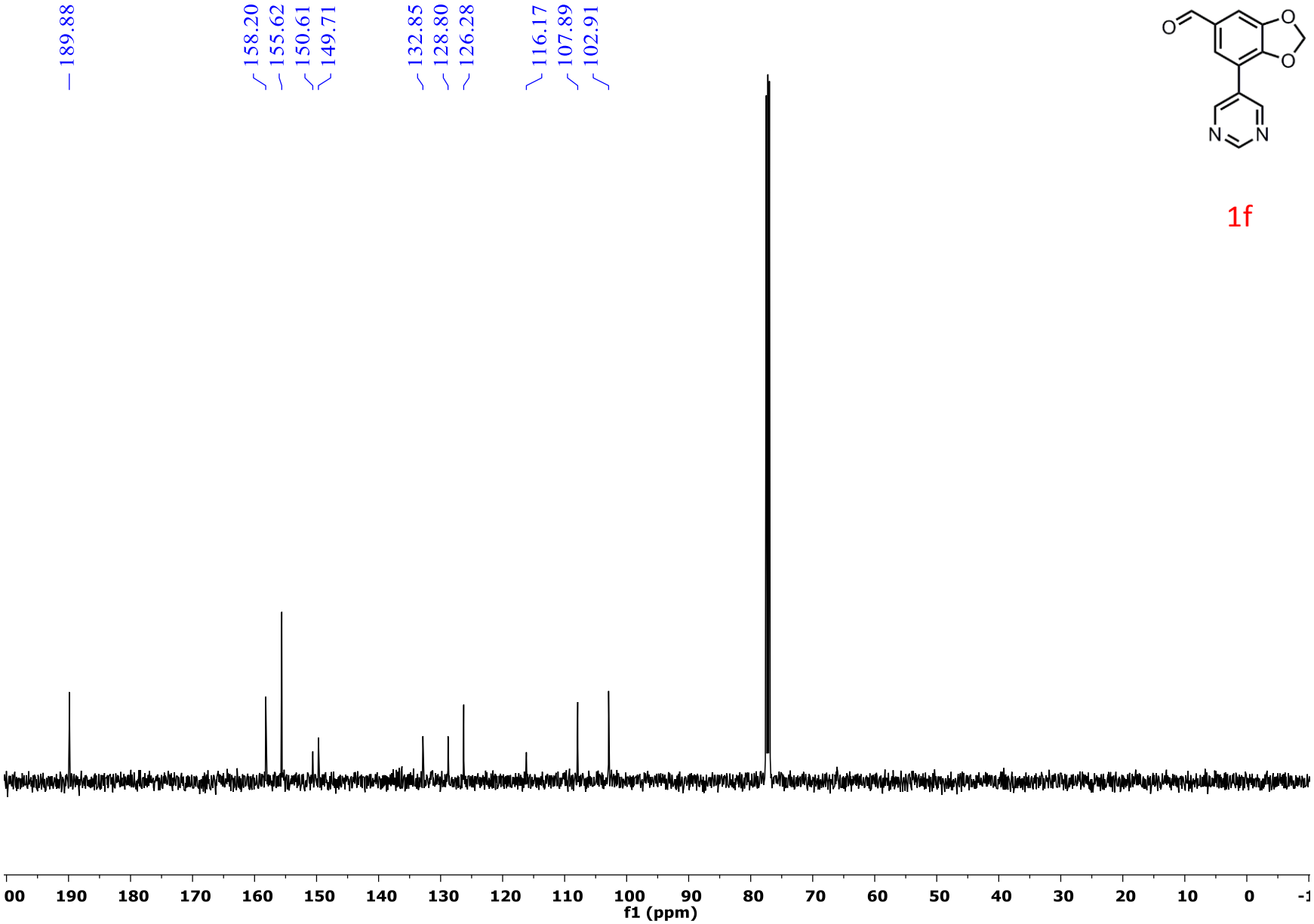

10.4859
9.0079
8.5657
8.4601
8.4560
8.4414
8.4372
8.2871
8.2828
8.2697
8.2653
7.1262
7.1086
3.9830
1.00
1.07
1.01
2.09
1.09
1.10
3.57
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)
O
O
N
N

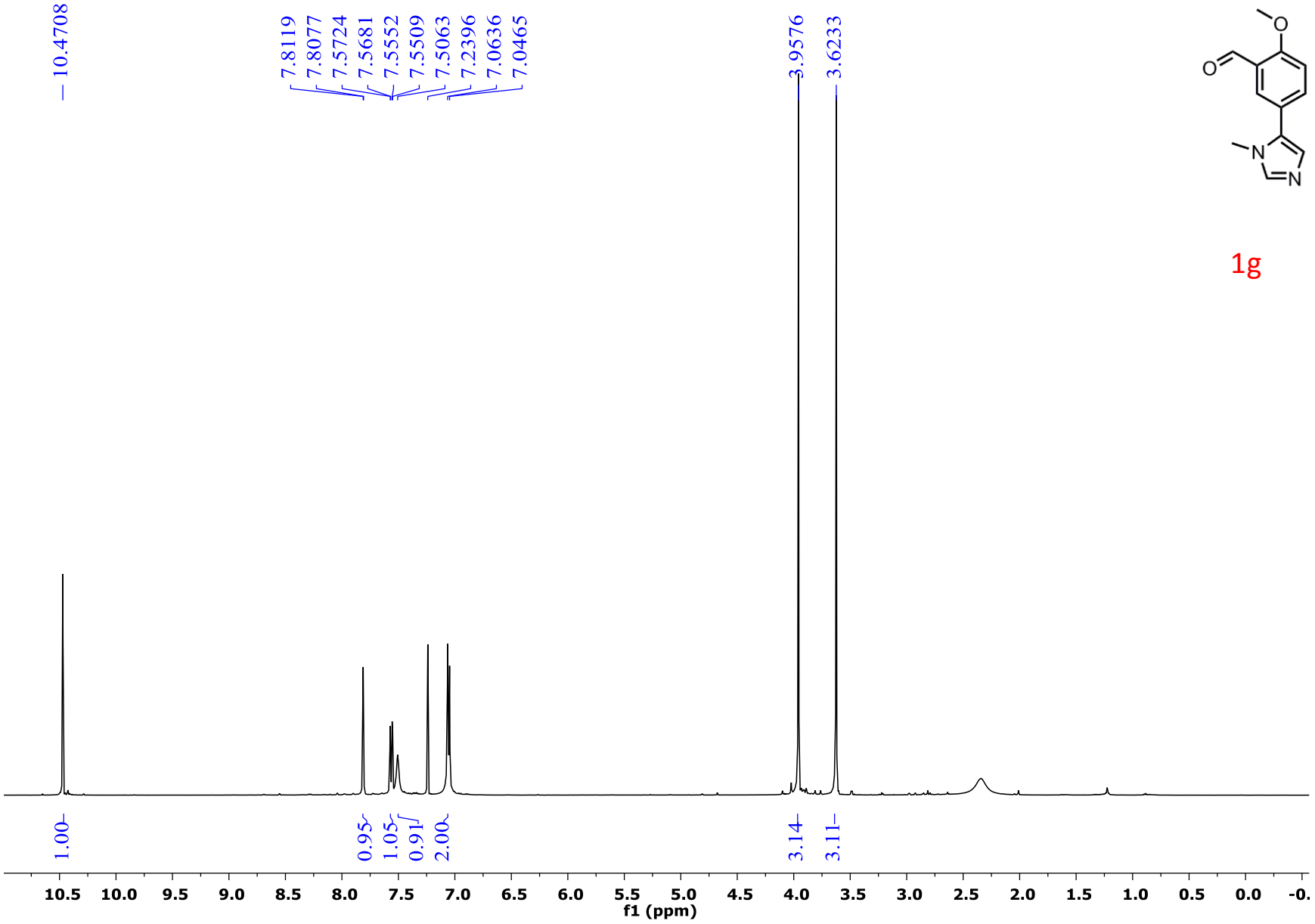
1e


189.39
163.12
151.52
144.25
143.00
141.80
134.53
129.24
127.11
125.19
112.67
56.18
O
O
N
N
1e
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

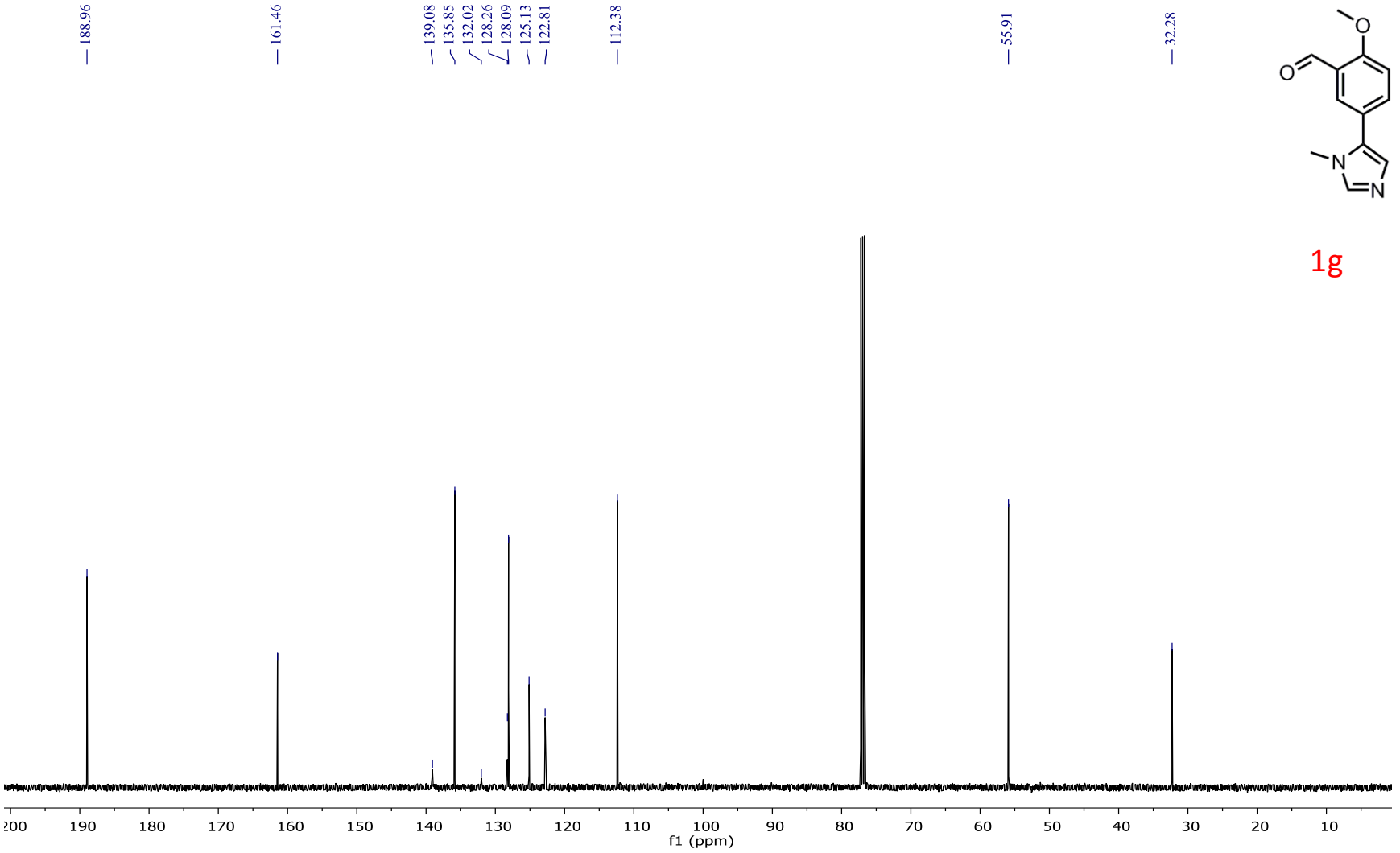

9.8907
9.2071
9.1037
7.6259
7.6230
7.3884
7.3855
6.1940
1.00
0.94
1.82
0.96
0.96
1.91
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
O
O
O
N
N

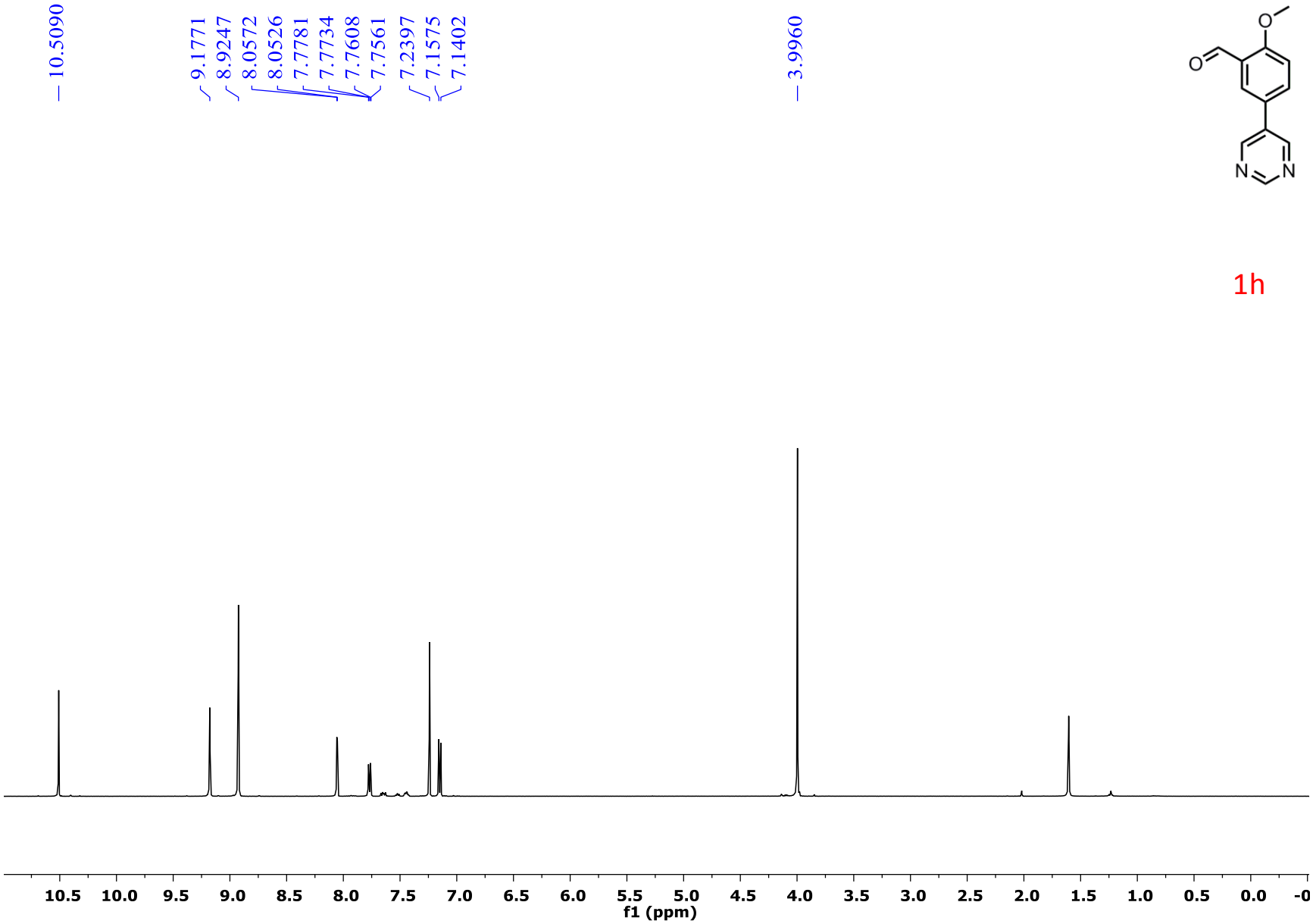
1f

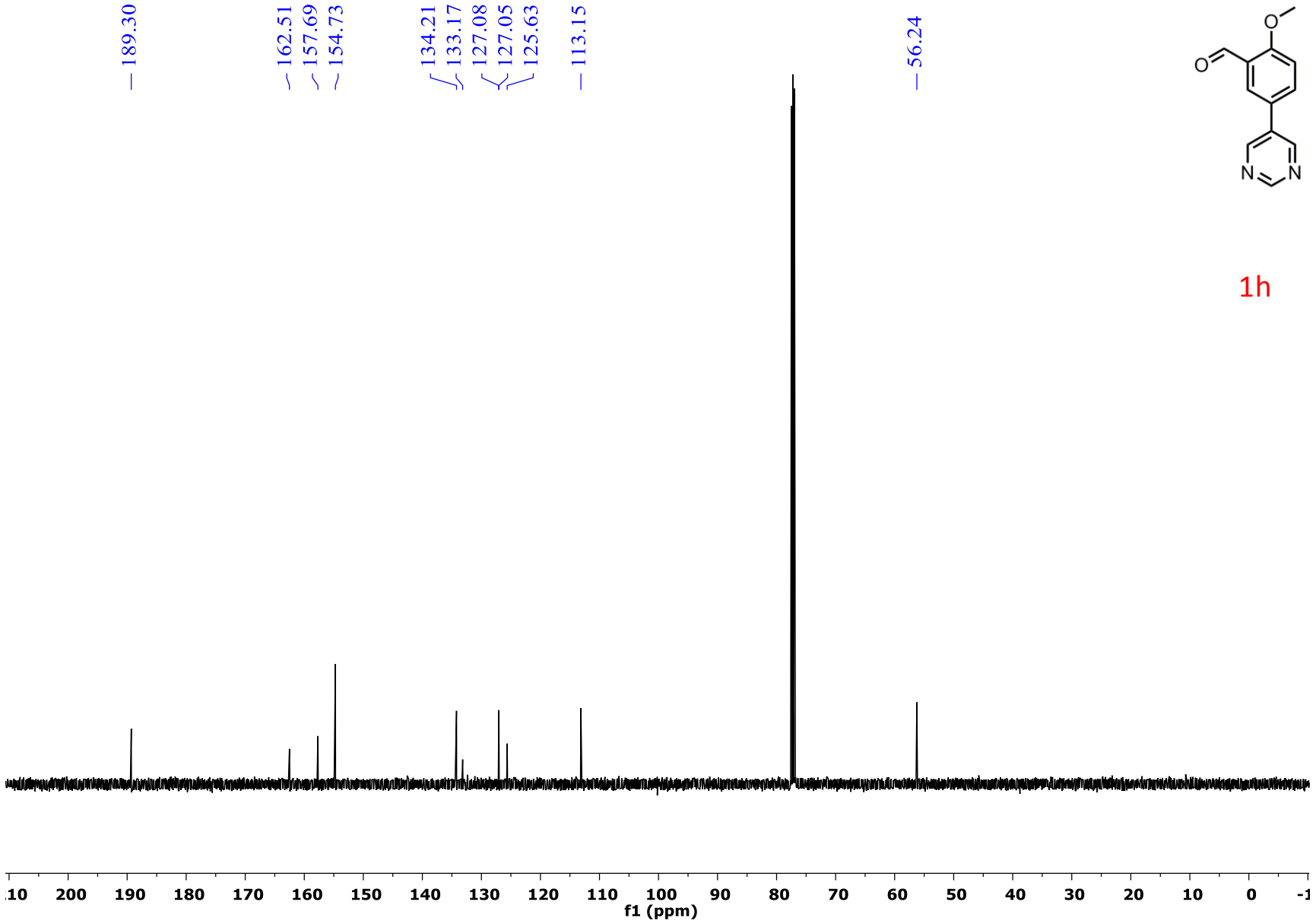

189.88
158.20
155.62
150.61
149.71
132.85
128.80
126.28
116.17
107.89
102.91
O
O
O
N
N
1f
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

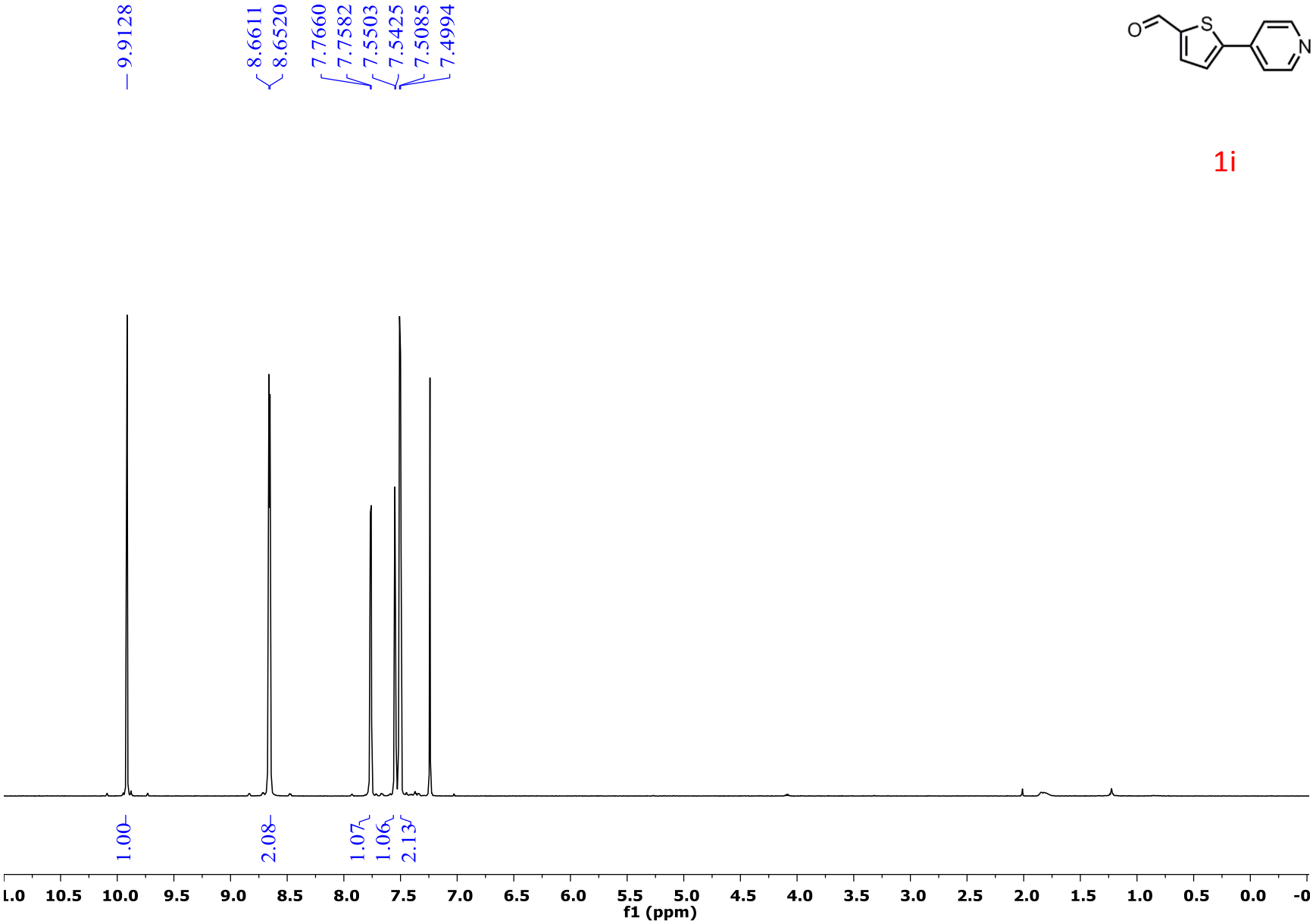

10.4708
7.8119
7.8077
7.5724
7.5681
7.5552
7.5509
7.5063
7.2396
7.0636
7.0465
3.9576
3.6233
1.00
0.95
1.05
0.91
2.00
3.14
3.11
f1 (ppm)

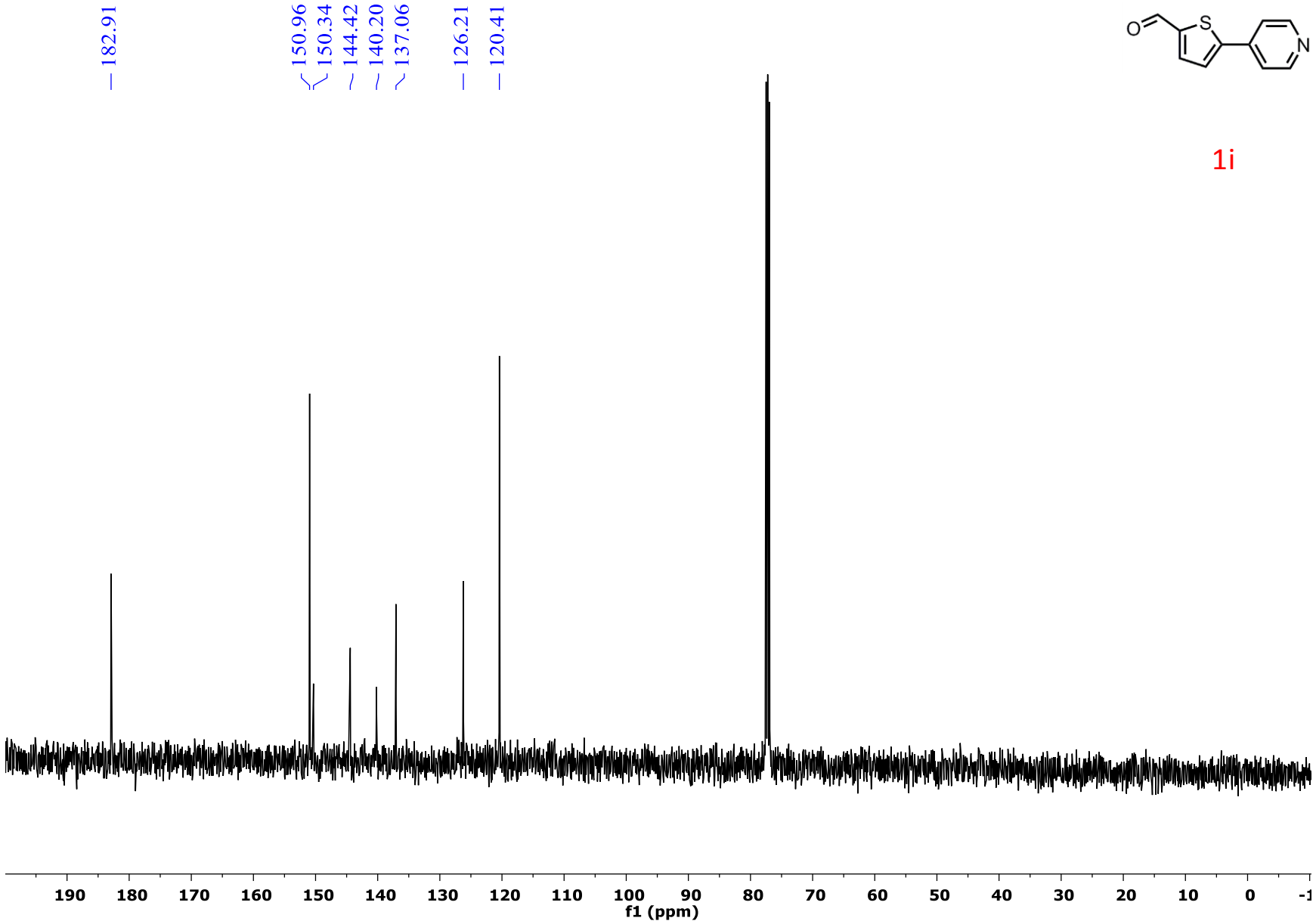
1g

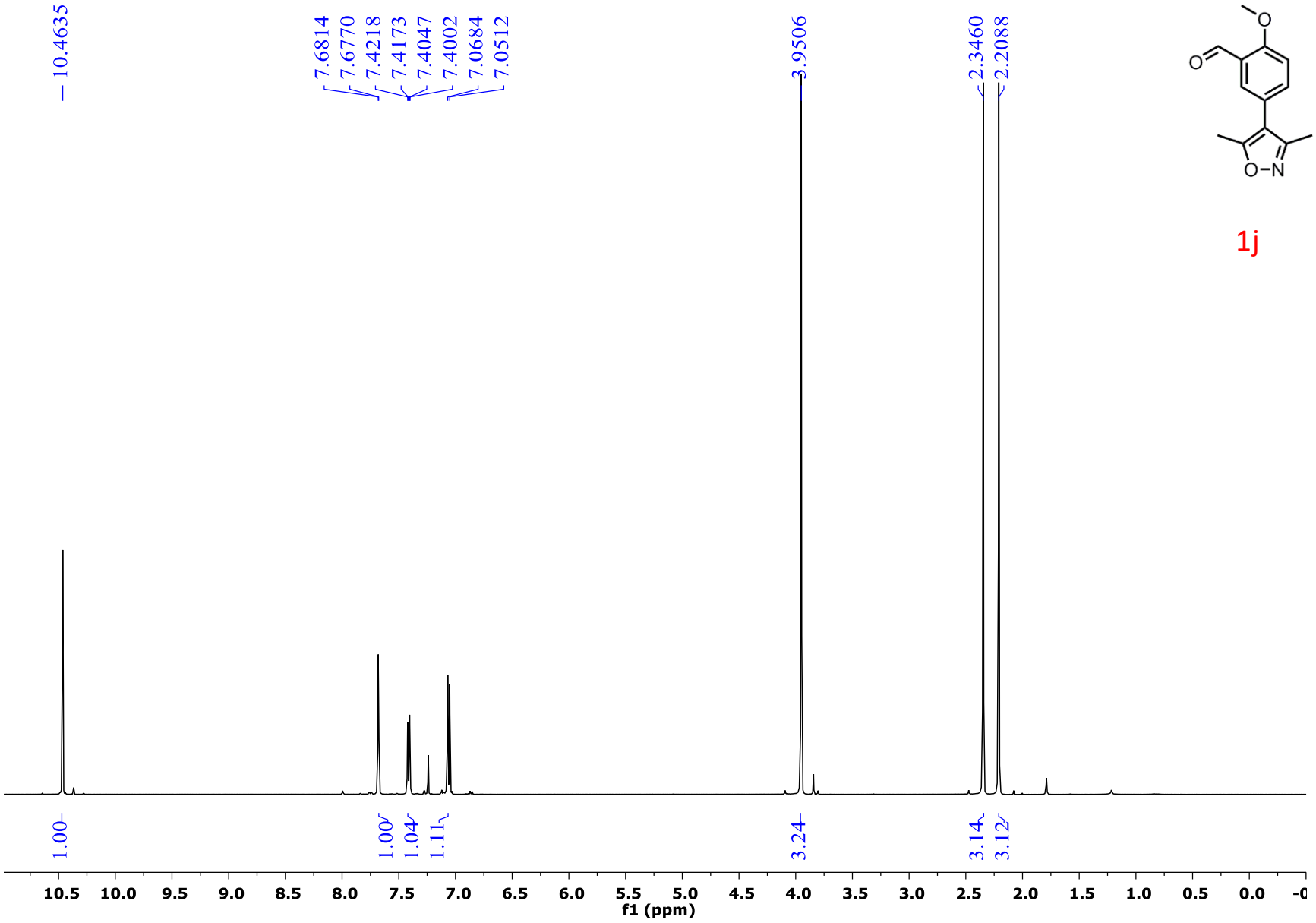

188.96
161.46
139.08
135.85
132.02
128.26
128.09
125.13
122.81
112.38
55.91
32.28
O
O
N
N
1g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


10.5090
9.1771
8.9247
8.0572
8.0526
7.7781
7.7734
7.7608
7.7561
7.2397
7.1575
7.1402
3.9960
O
O
N
N
1h
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

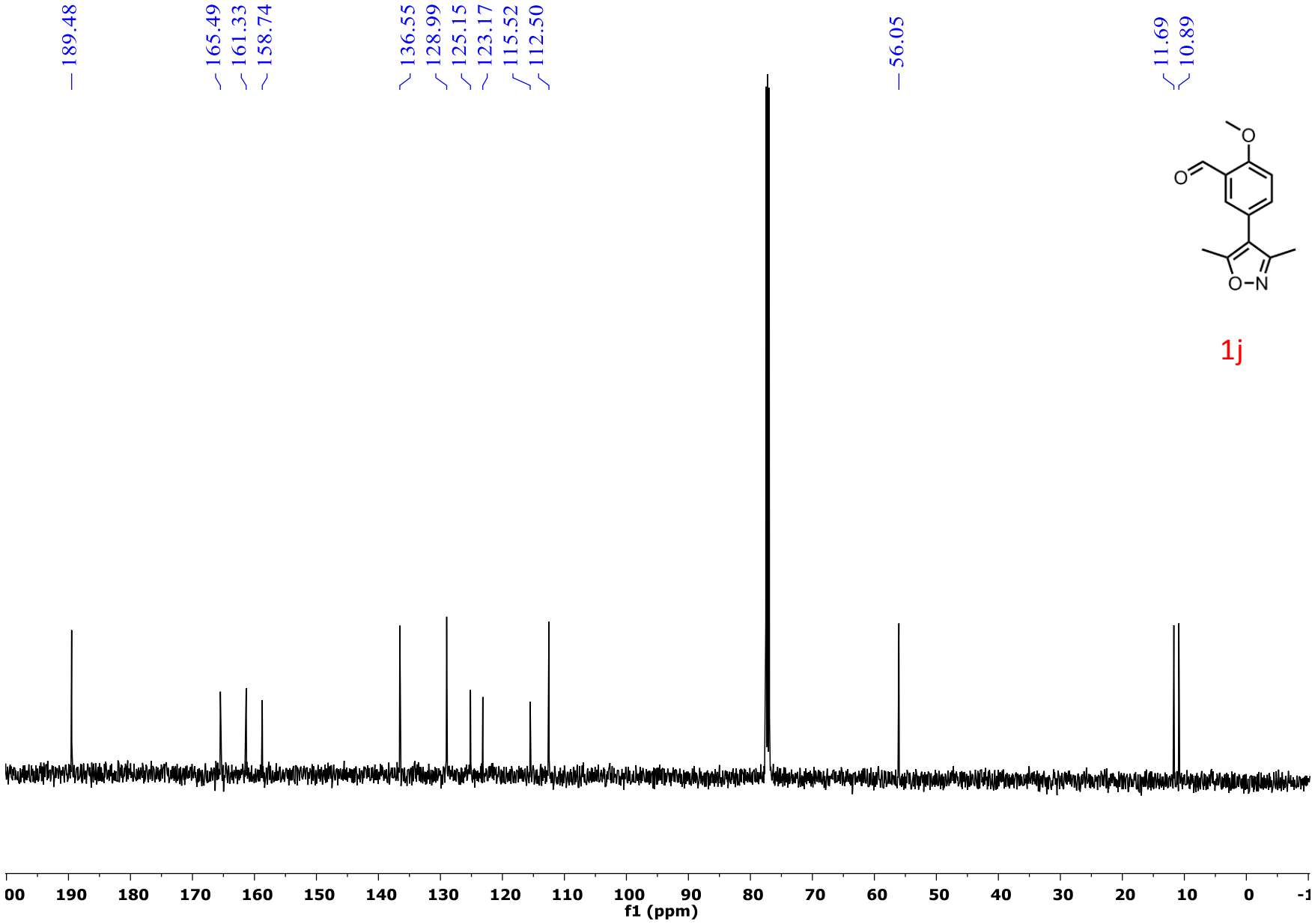

189.30
162.51
157.69
154.73
134.21
133.17
127.08
127.05
125.63
113.15
56.24
O
O
N
N
1h
f1 (ppm)

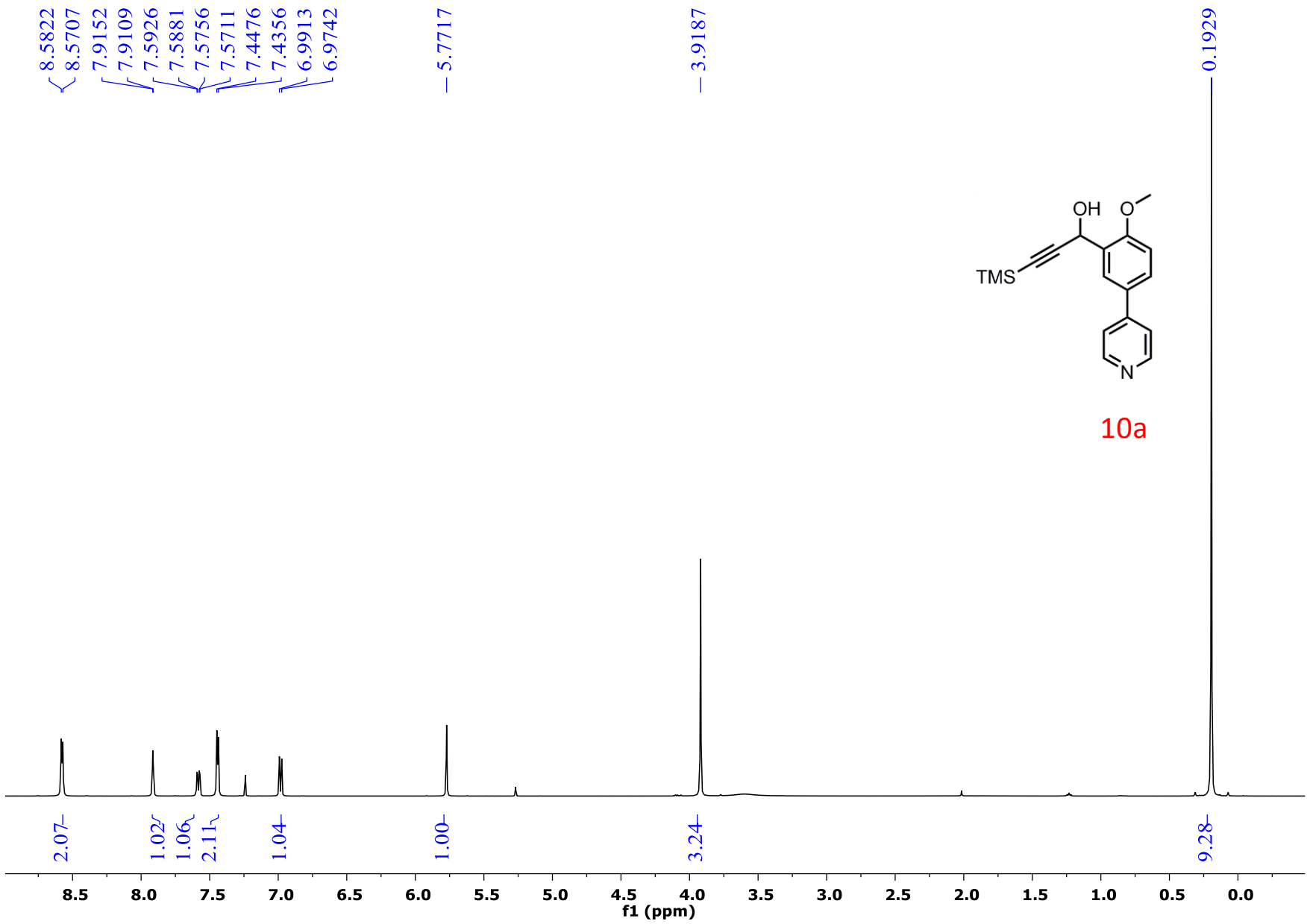

9.9128
8.6611
8.6520
7.7660
7.7582
7.5503
7.5425
7.5085
7.4994
O
S
N
1i
1.00
2.08
1.07
1.06
2.13
f1 (ppm)

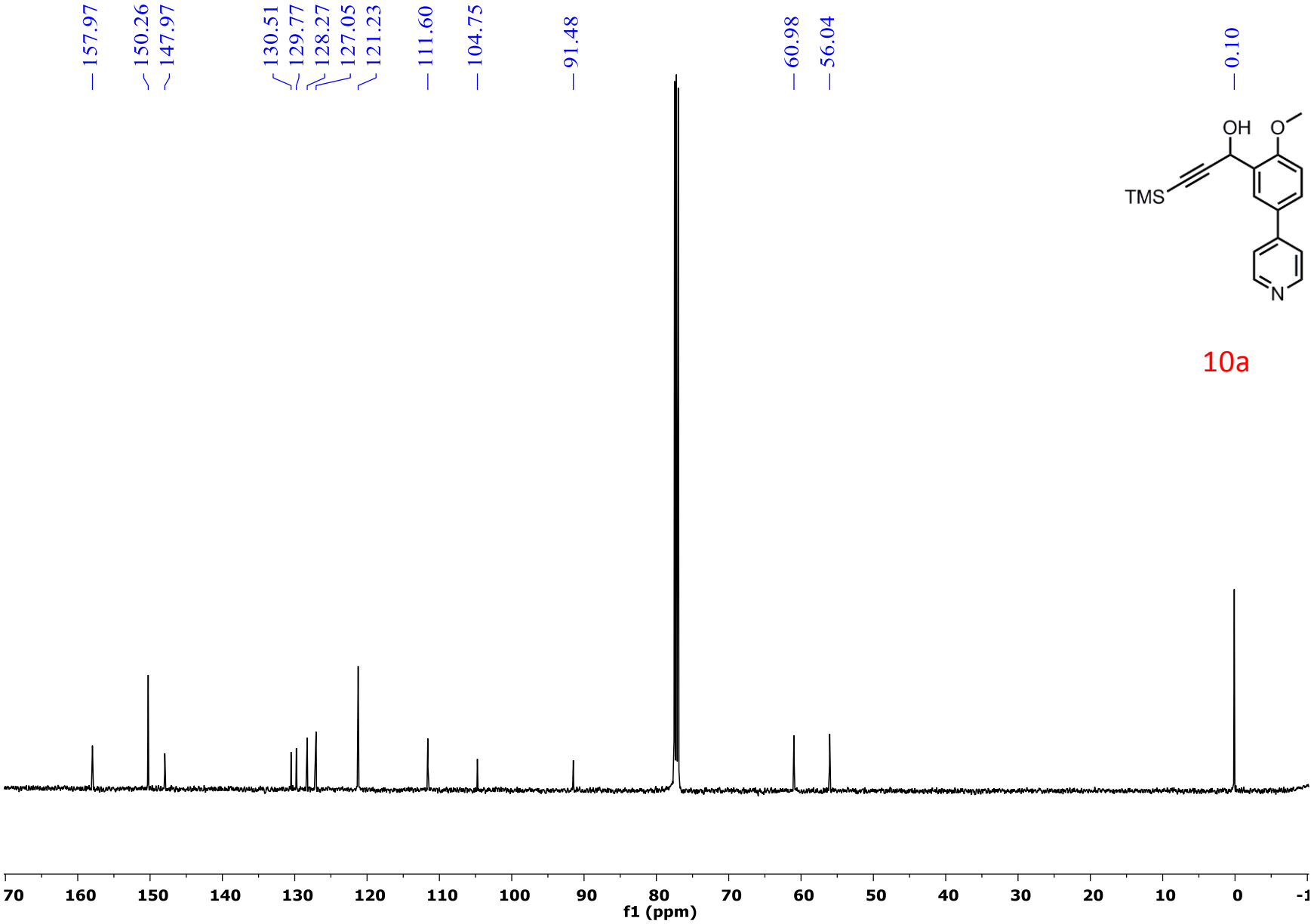

182.91
150.96
150.34
144.42
140.20
137.06
126.21
120.41
O
S
N
1i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

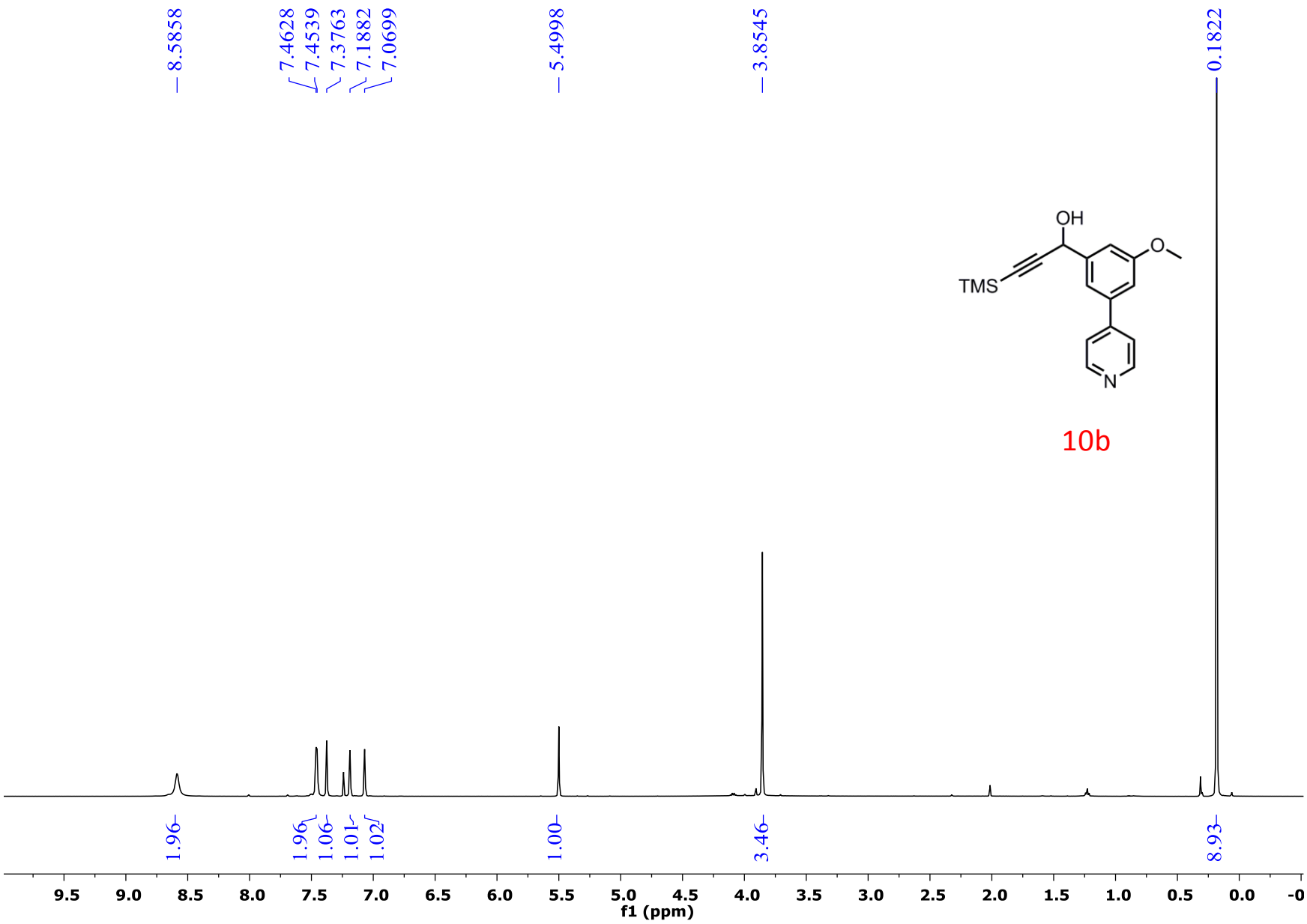

10.4635
7.6814
7.6770
7.4218
7.4173
7.4047
7.4002
7.0684
7.0512
3.9506
2.3460
2.2088
1.00
1.00
1.04
1.11
3.24
3.14
3.12
f1 (ppm)

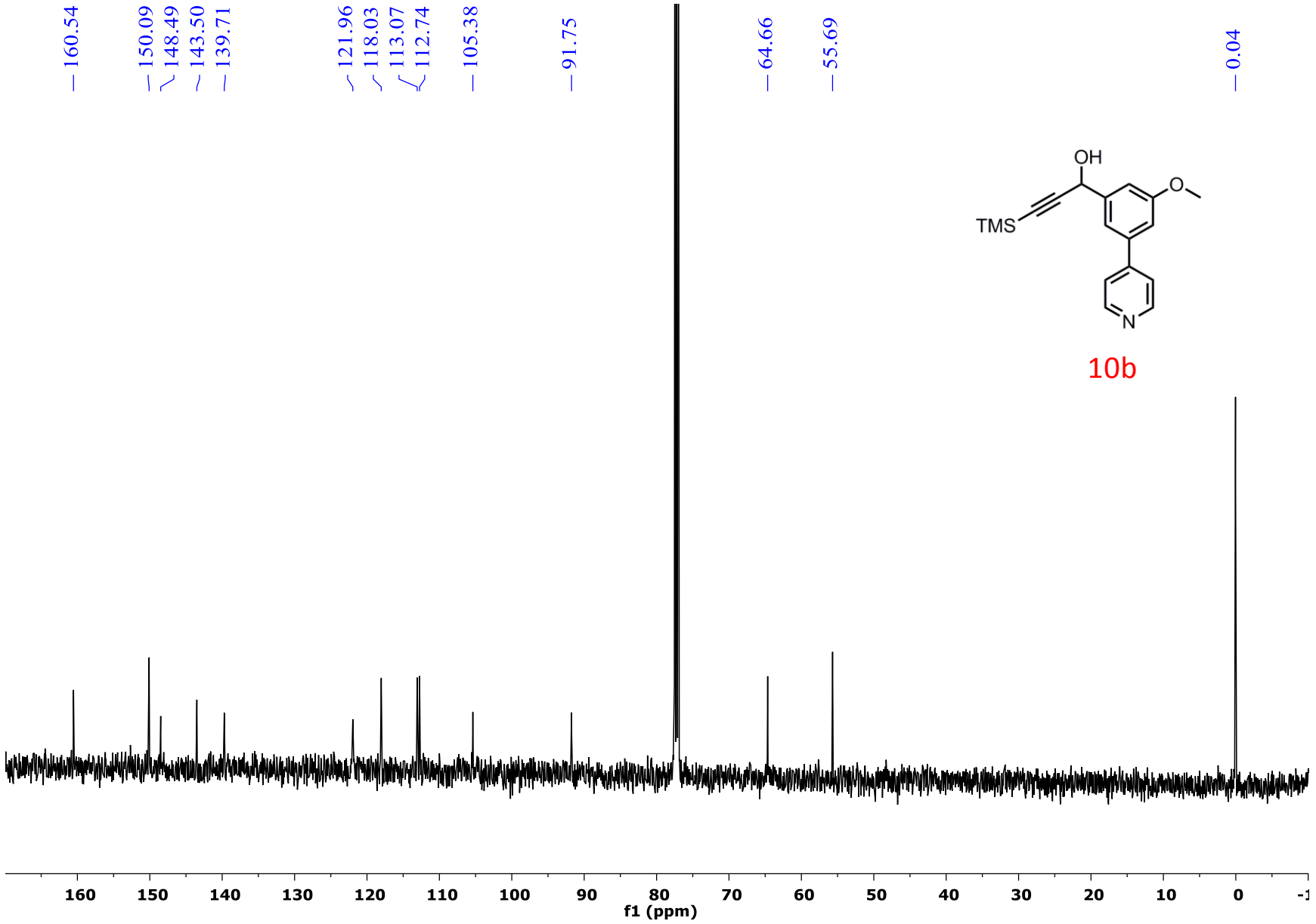
1j

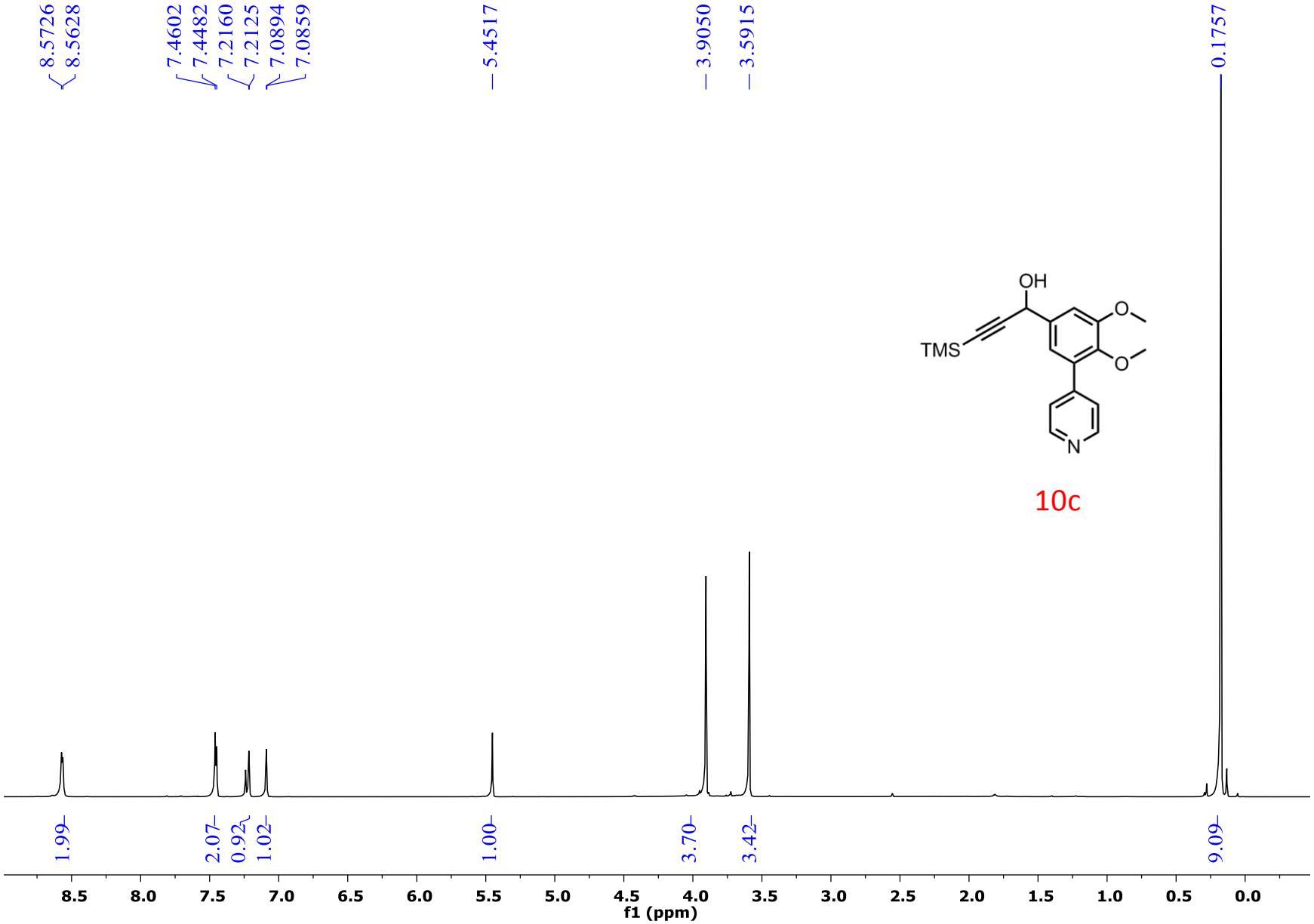

189.48
165.49
161.33
158.74
136.55
128.99
125.15
123.17
115.52
112.50
56.05
11.69
10.89
O
O
O–N
1j
f1 (ppm)

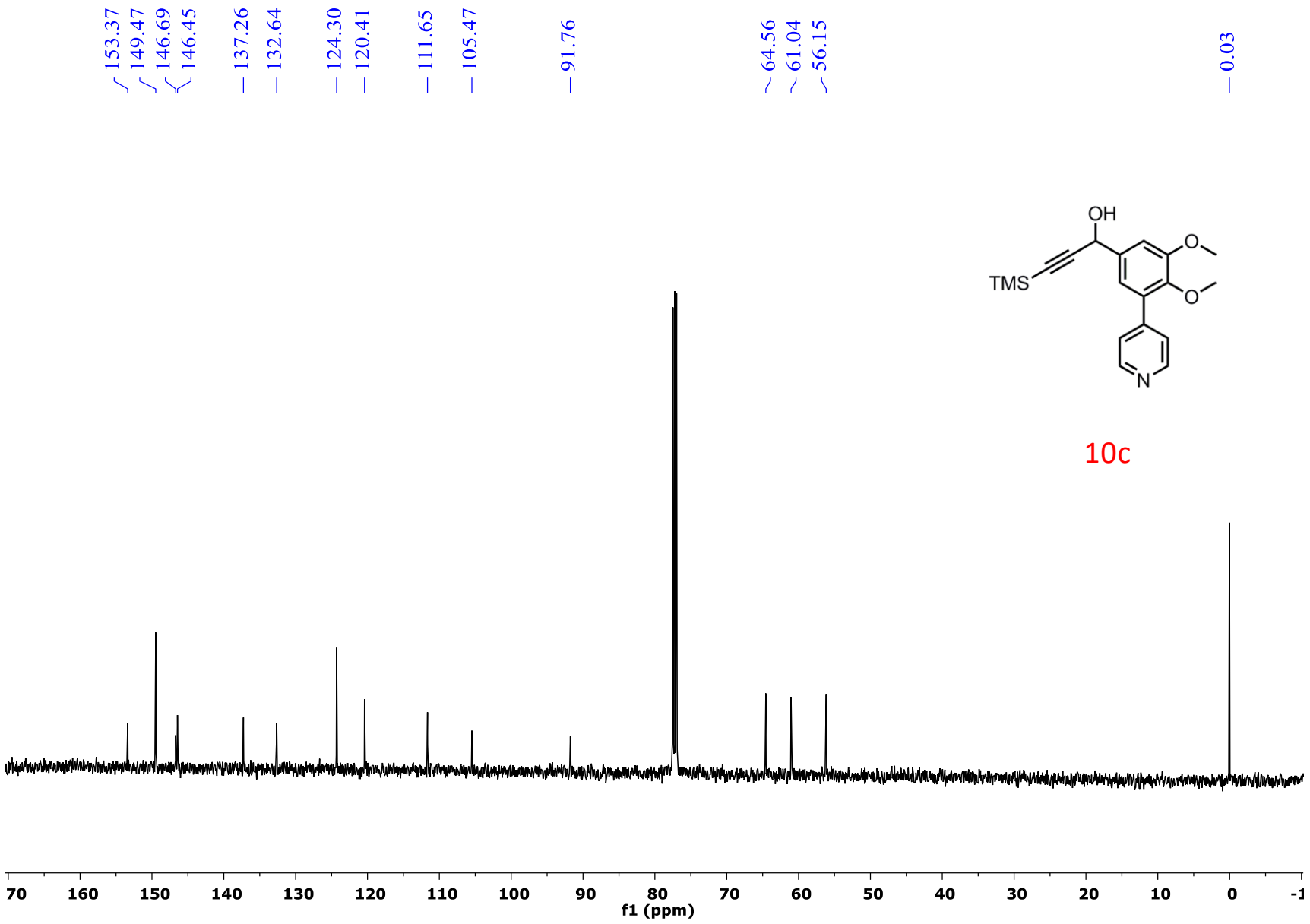

8.5822
8.5707
7.9152
7.9109
7.5926
7.5881
7.5756
7.5711
7.4476
7.4356
6.9913
6.9742
5.7717
3.9187
0.1929
OH
O
TMS
N
10a
2.07
1.02
1.06
2.11
1.04
1.00
3.24
9.28
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

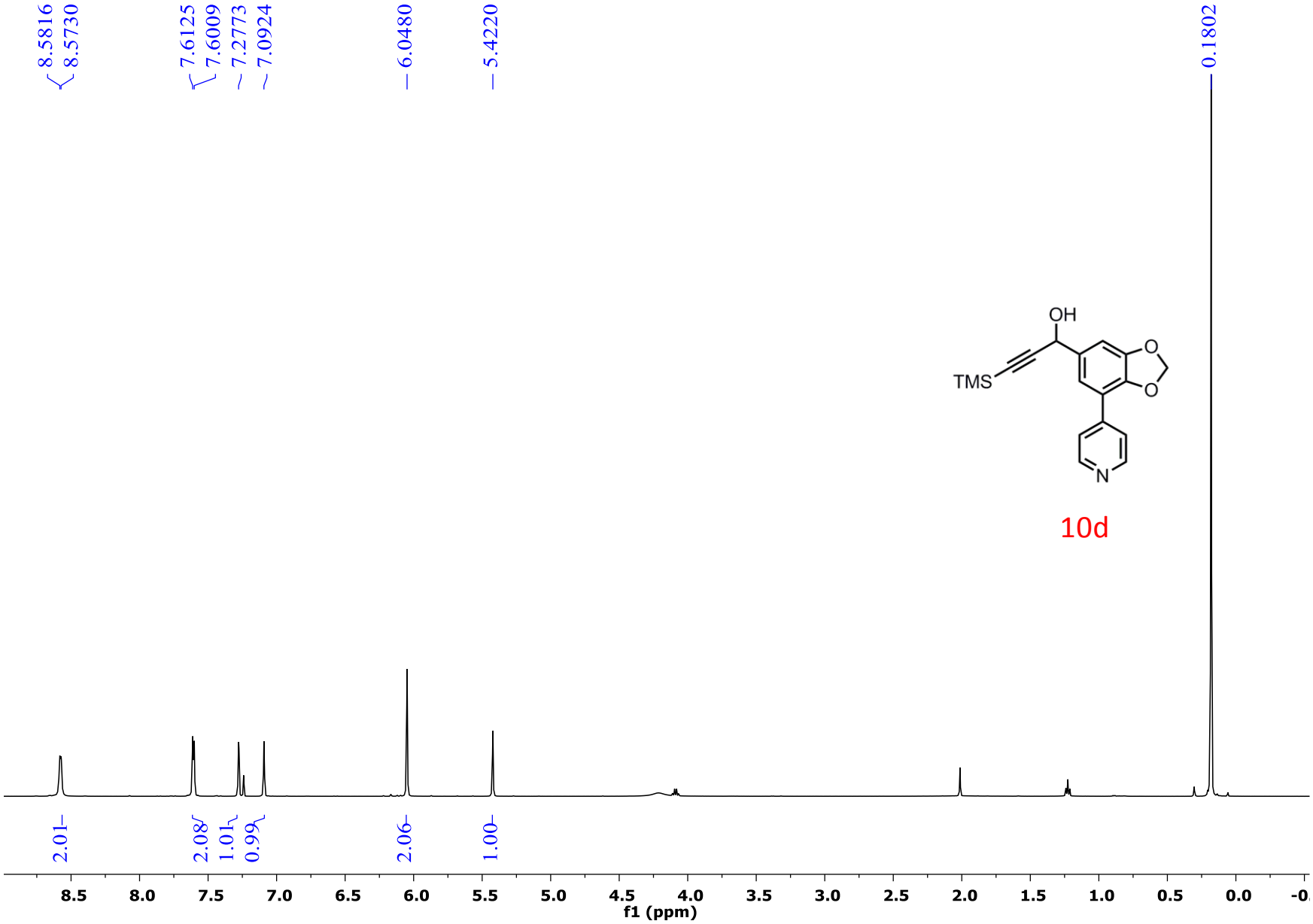

157.97
150.26
147.97
130.51
129.77
128.27
127.05
121.23
111.60
104.75
91.48
60.98
56.04
0.10
OH
O
TMS
N
10a
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

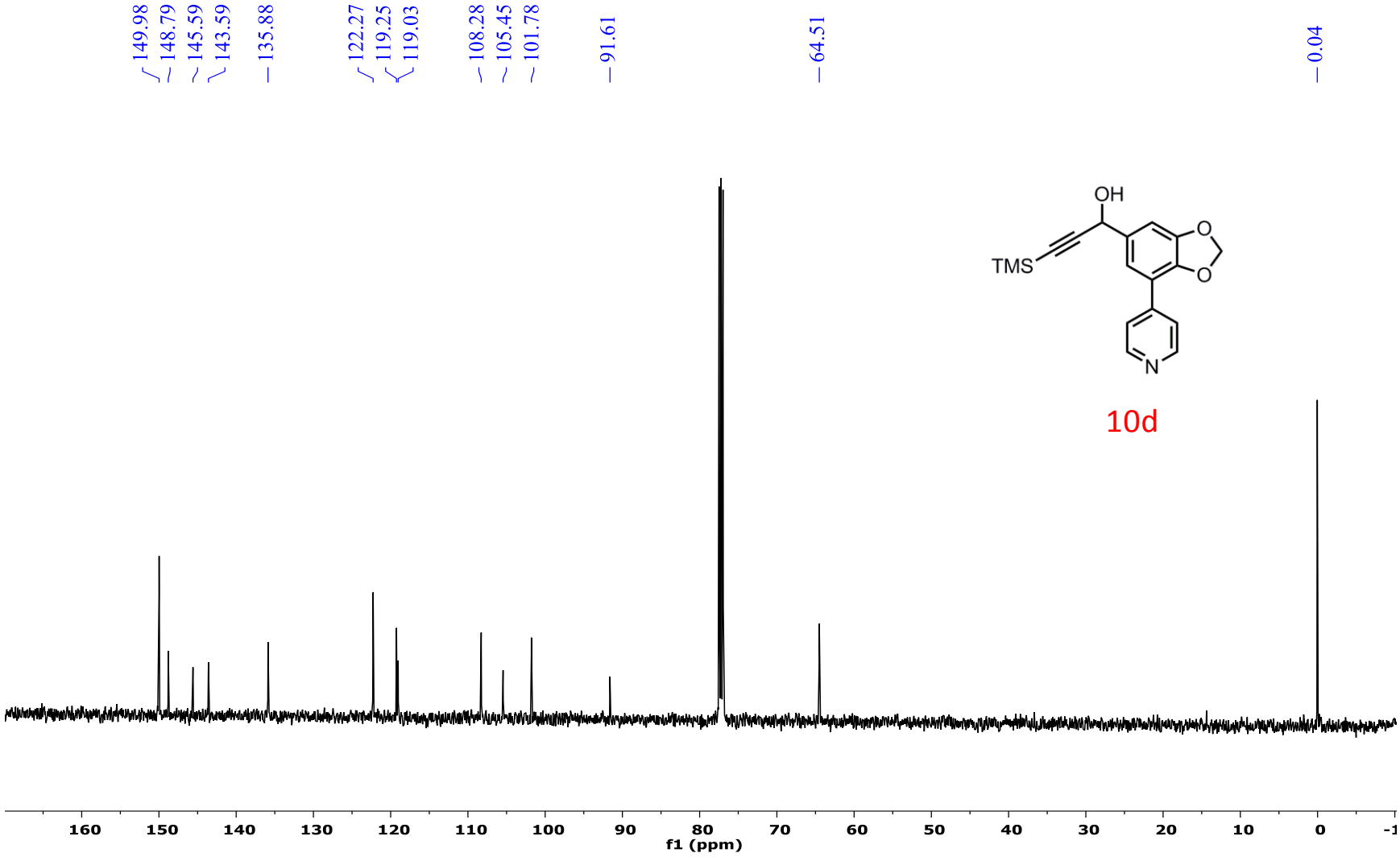

8.5858
7.4628
7.4539
7.3763
7.1882
7.0699
5.4998
3.8545
0.1822
OH
TMS
O
N
10b
1.96
1.96
1.06
1.01
1.02
1.00
3.46
8.93
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

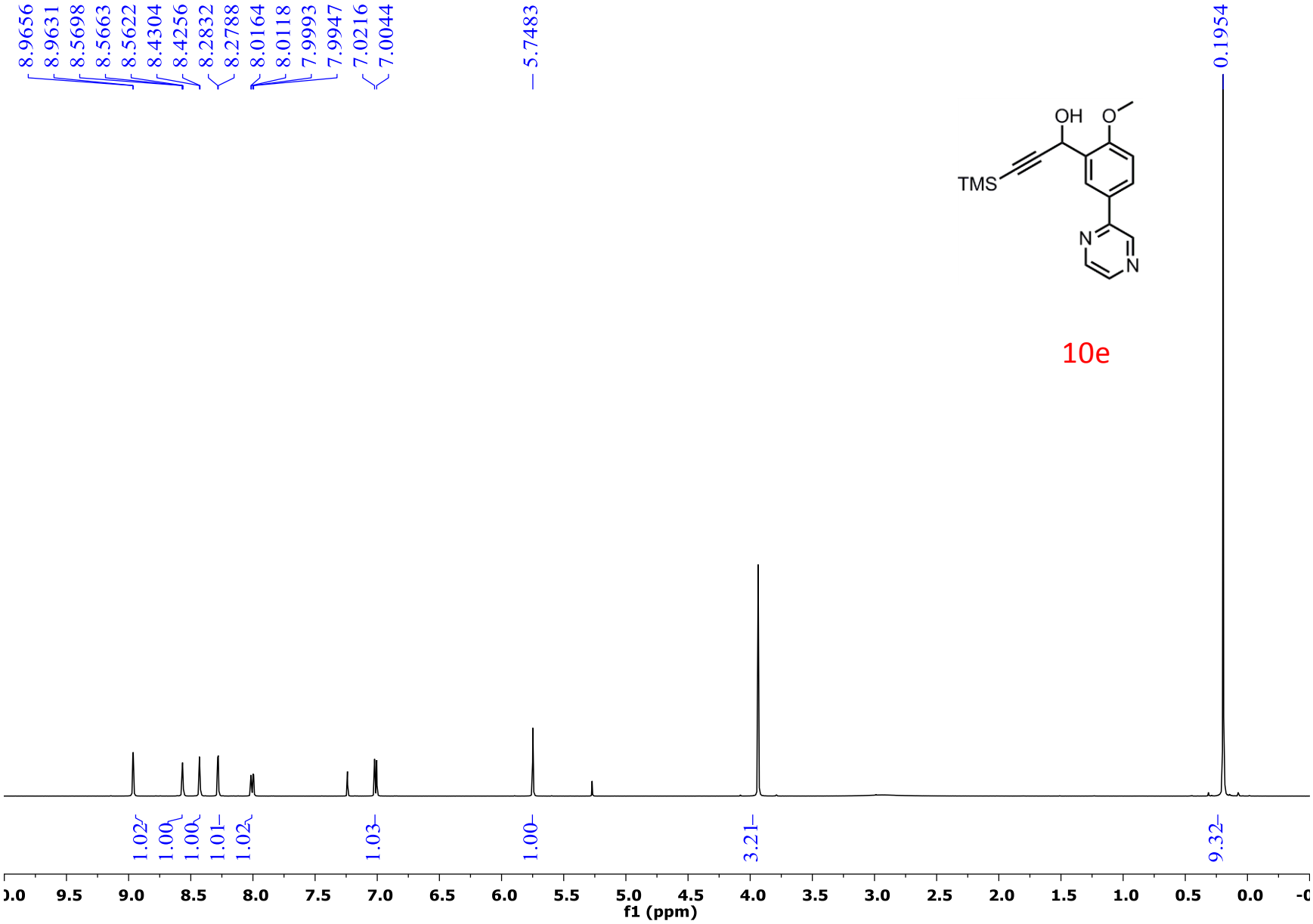

160.54
150.09
148.49
143.50
139.71
121.96
118.03
113.07
112.74
105.38
91.75
64.66
55.69
0.04
OH
TMS
O
N
10b
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

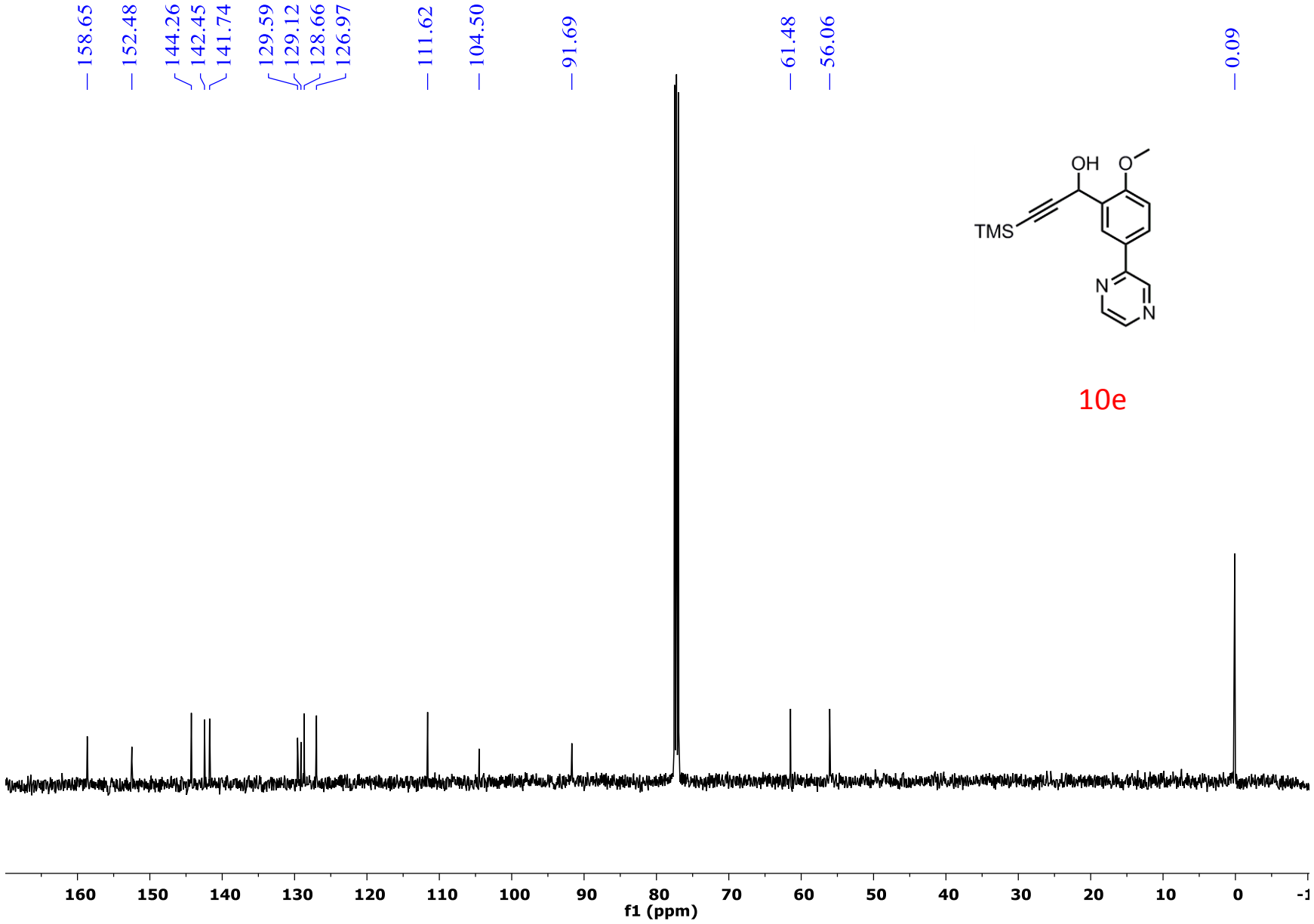

8.5726
8.5628
7.4602
7.4482
7.2160
7.2125
7.0894
7.0859
5.4517
3.9050
3.5915
0.1757
OH
TMS
O
O
N
10c
1.99
2.07
0.92
1.02
1.00
3.70
3.42
9.09
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

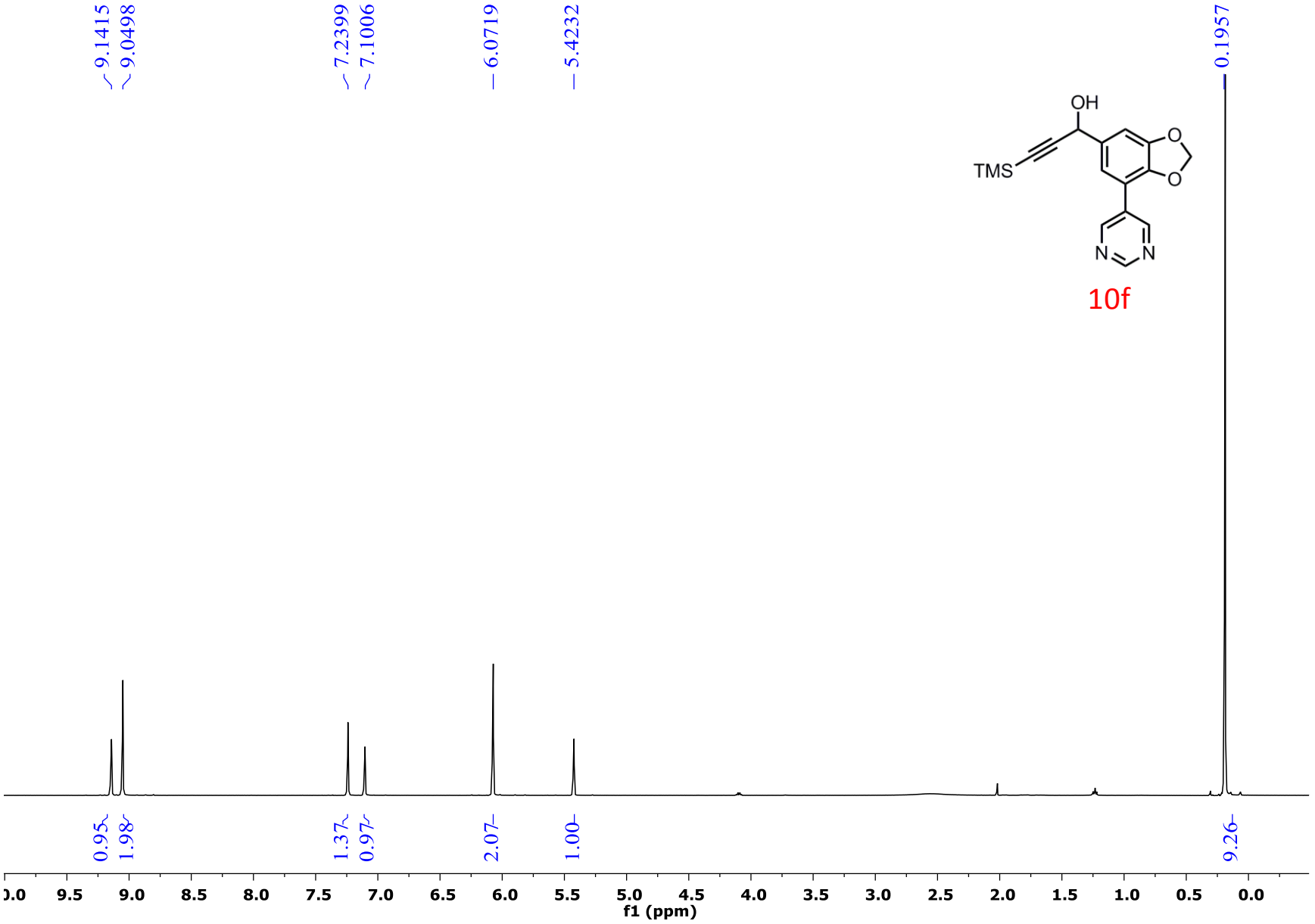

153.37
149.47
146.69
146.45
137.26
132.64
124.30
120.41
111.65
105.47
91.76
64.56
61.04
56.15
0.03
OH
TMS
O
O
N
10c
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

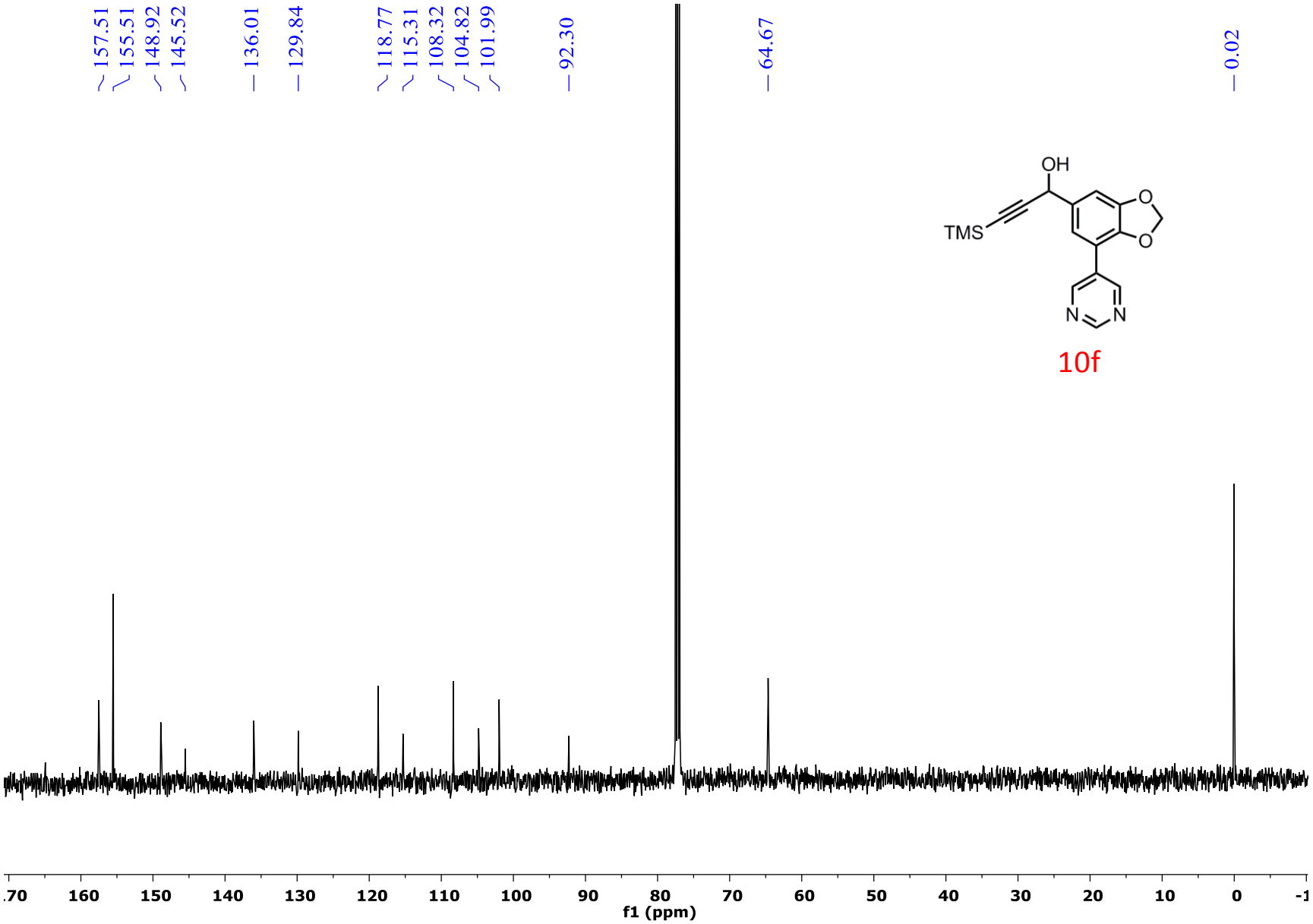

8.5816
8.5730
7.6125
7.6009
7.2773
7.0924
6.0480
5.4220
0.1802
OH
TMS
O
O
N
10d
2.01
2.08
1.01
0.99
2.06
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

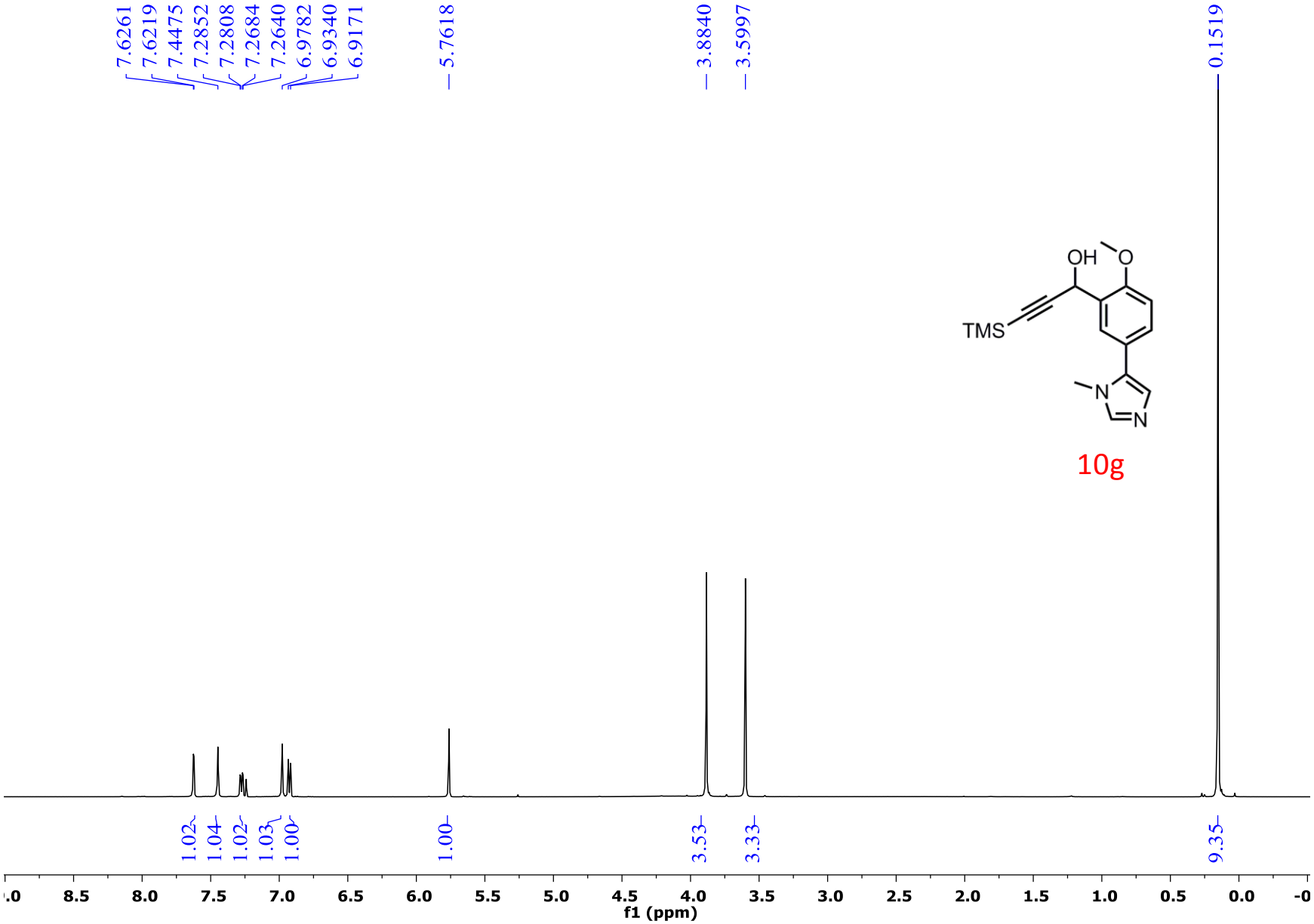

149.98
148.79
145.59
143.59
135.88
122.27
119.25
119.03
108.28
105.45
101.78
91.61
64.51
0.04
OH
TMS
O
O
N
10d
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

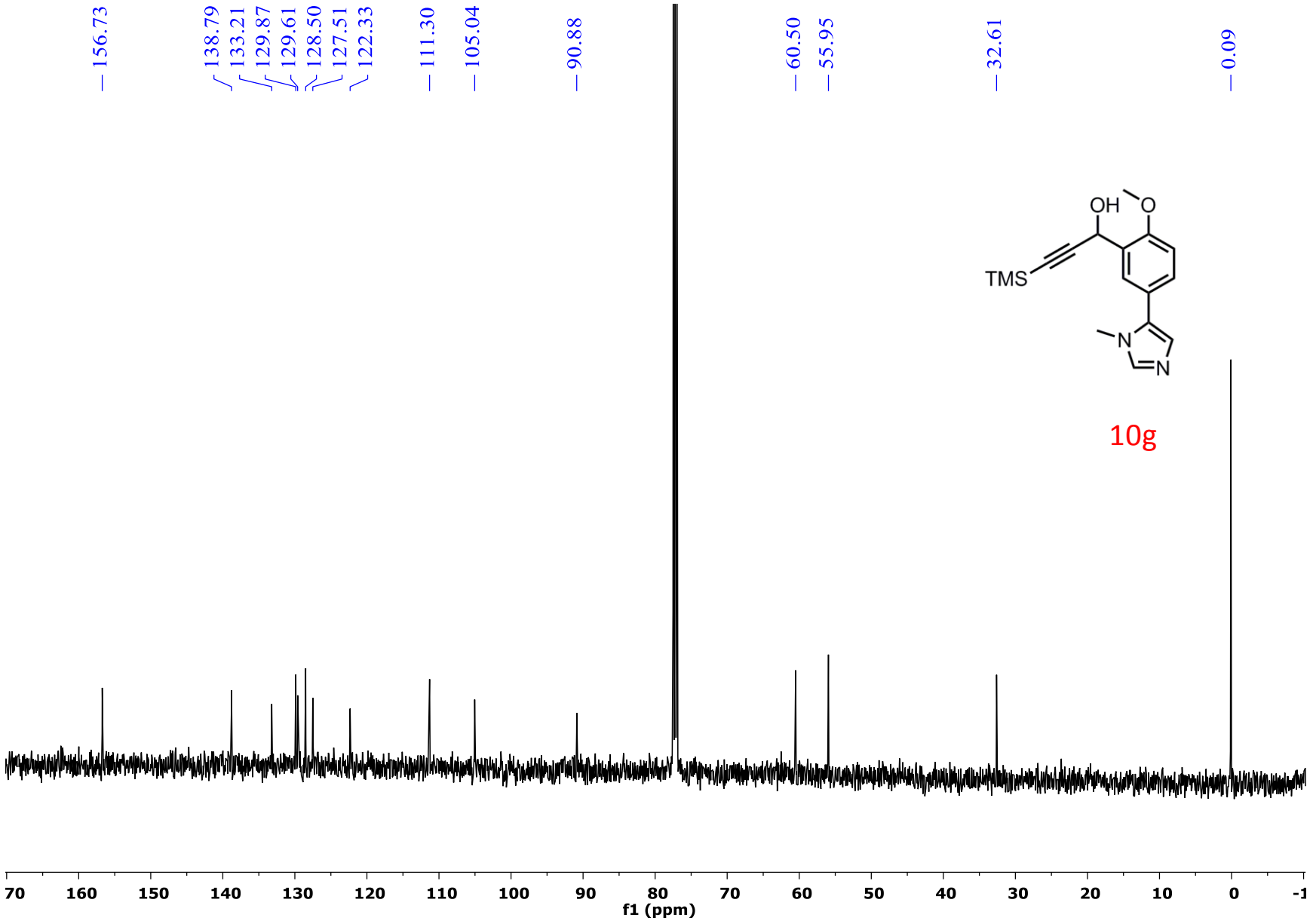

8.9656
8.9631
8.5698
8.5663
8.5622
8.4304
8.4256
8.2832
8.2788
8.0164
8.0118
7.9993
7.9947
7.0216
7.0044
5.7483
0.1954
OH
O
TMS
N
N
10e
1.02
1.00
1.00
1.01
1.02
1.03
1.00
3.21
9.32
f1 (ppm)

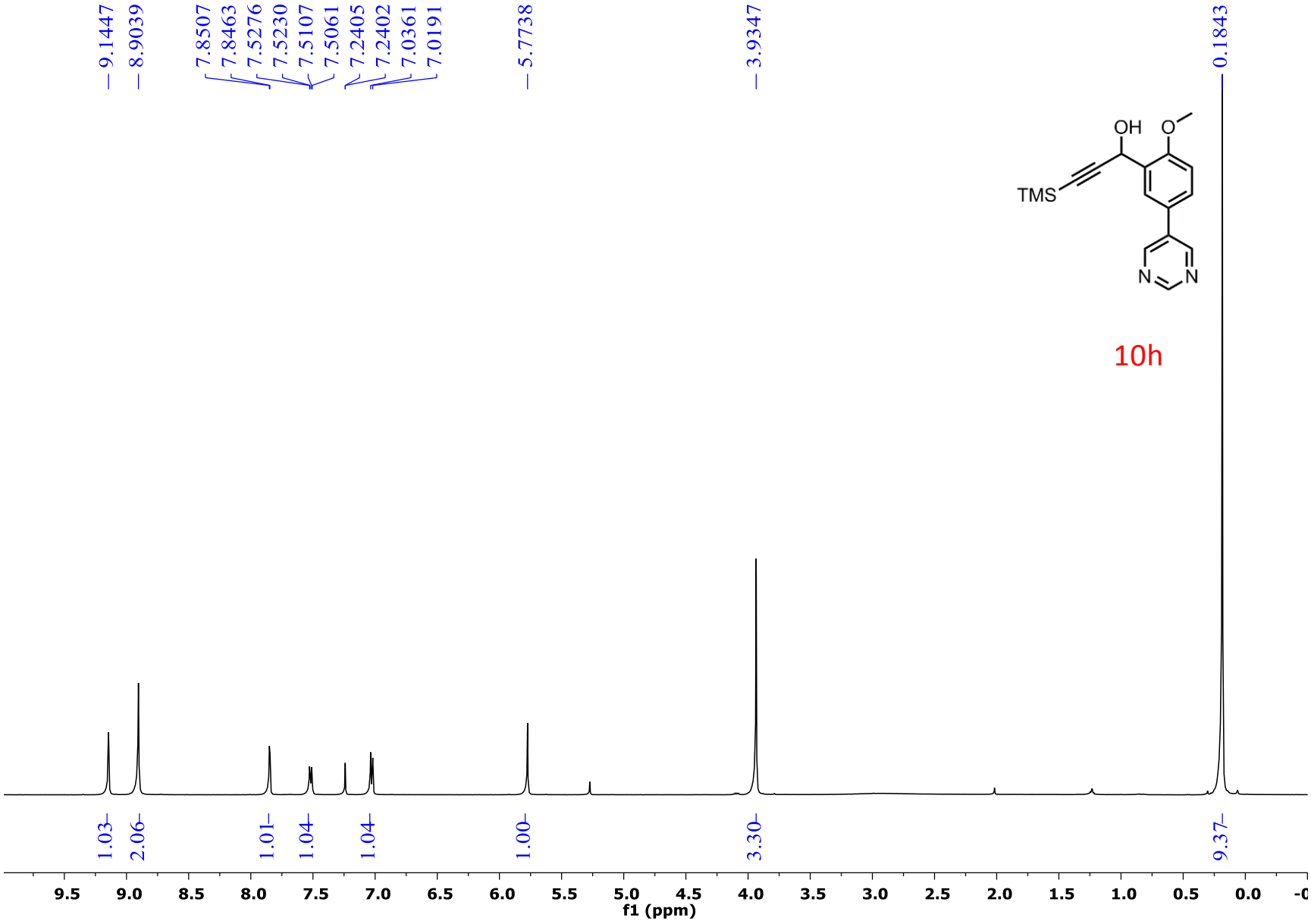

158.65
152.48
144.26
142.45
141.74
129.59
129.12
128.66
126.97
111.62
104.50
91.69
61.48
56.06
0.09
OH
O
TMS
N
N
10e
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


9.1415
9.0498
7.2399
7.1006
6.0719
5.4232
0.1957
OH
TMS
O
O
N
N
10f
0.95
1.98
1.37
0.97
2.07
1.00
9.26
f1 (ppm)


157.51
155.51
148.92
145.52
136.01
129.84
118.77
115.31
108.32
104.82
101.99
92.30
64.67
0.02
OH
TMS
O
O
N
N
10f
f1 (ppm)


7.6261
7.6219
7.4475
7.2852
7.2808
7.2684
7.2640
6.9782
6.9340
6.9171
5.7618
3.8840
3.5997
0.1519
OH
O
TMS
N
N
10g
1.02
1.04
1.02
1.03
1.00
1.00
3.53
3.33
9.35
f1 (ppm)


156.73
138.79
133.21
129.87
129.61
128.50
127.51
122.33
111.30
105.04
90.88
60.50
55.95
32.61
0.09
OH
O
TMS
N
N
10g
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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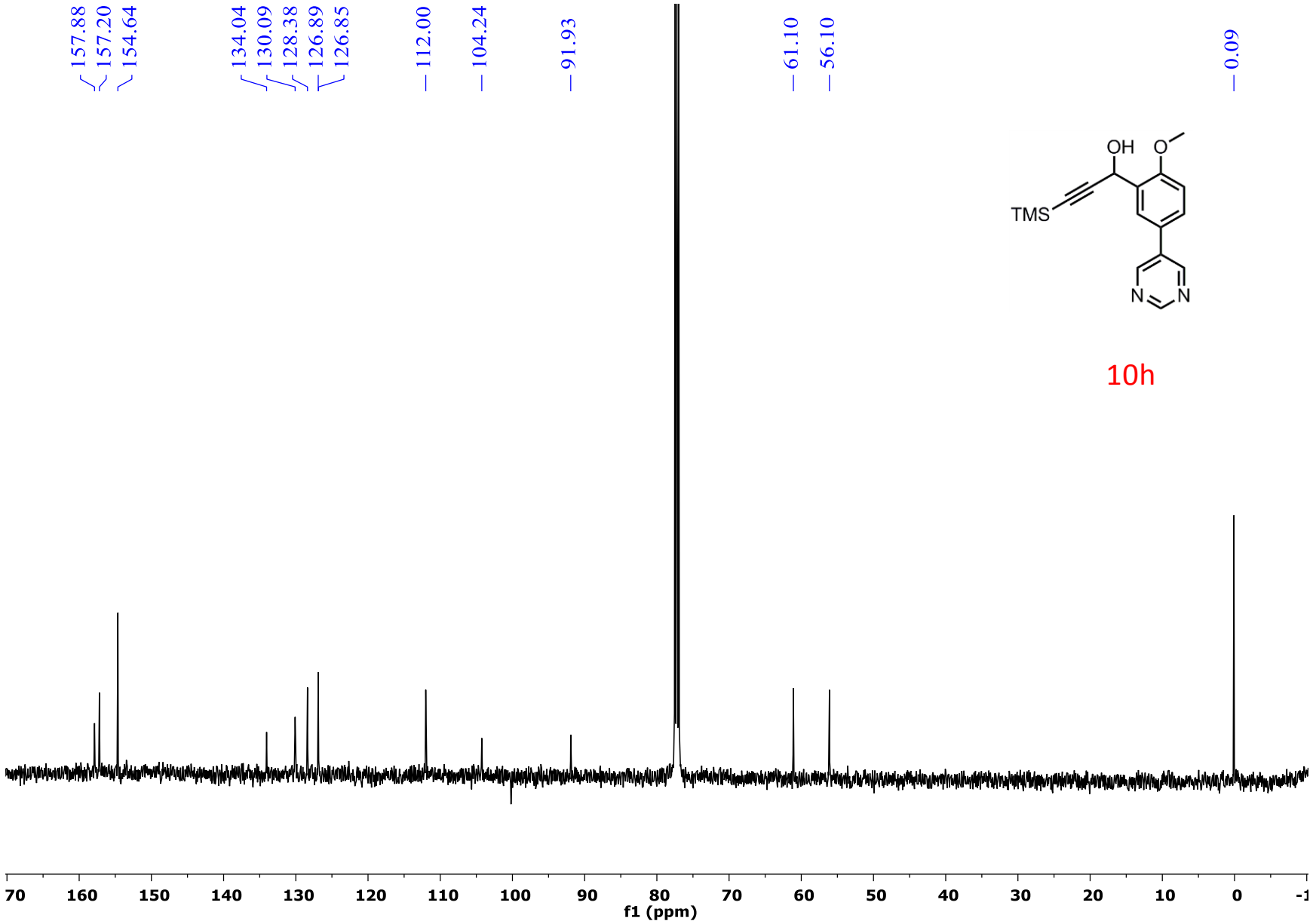
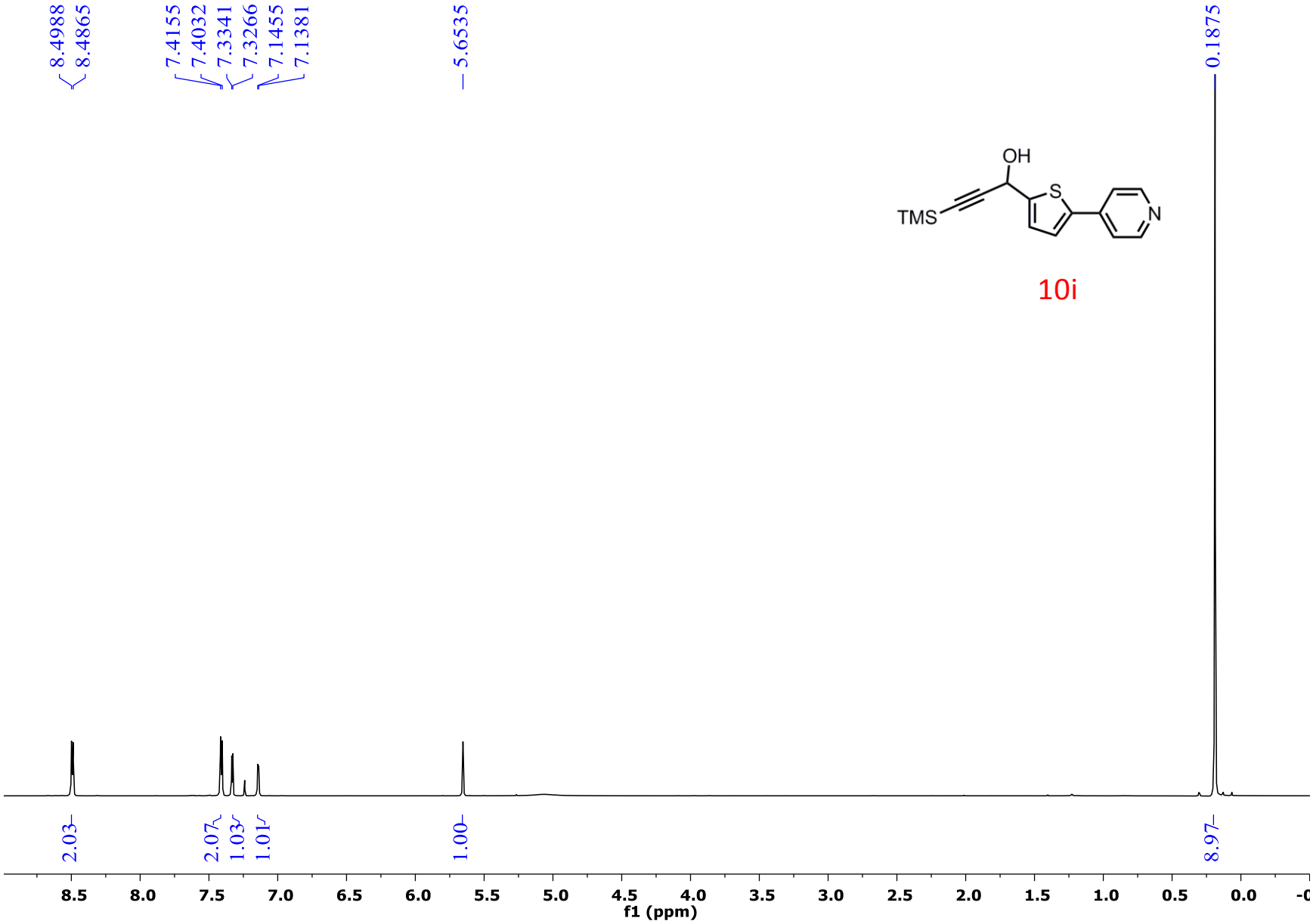
8.9039
7.8507
7.8463
7.5276
7.5230
7.5107
7.5061
7.2405
7.2402
7.0361
7.0191
5.7738
3.9347
0.1843
OH
O
TMS
N
N
10h
1.03
2.06
1.01
1.04
1.04
1.00
3.30
9.37
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.88
157.20
154.64
134.04
130.09
128.38
126.89
126.85
112.00
104.24
91.93
61.10
56.10
0.09
OH
O
TMS
N
N
10h
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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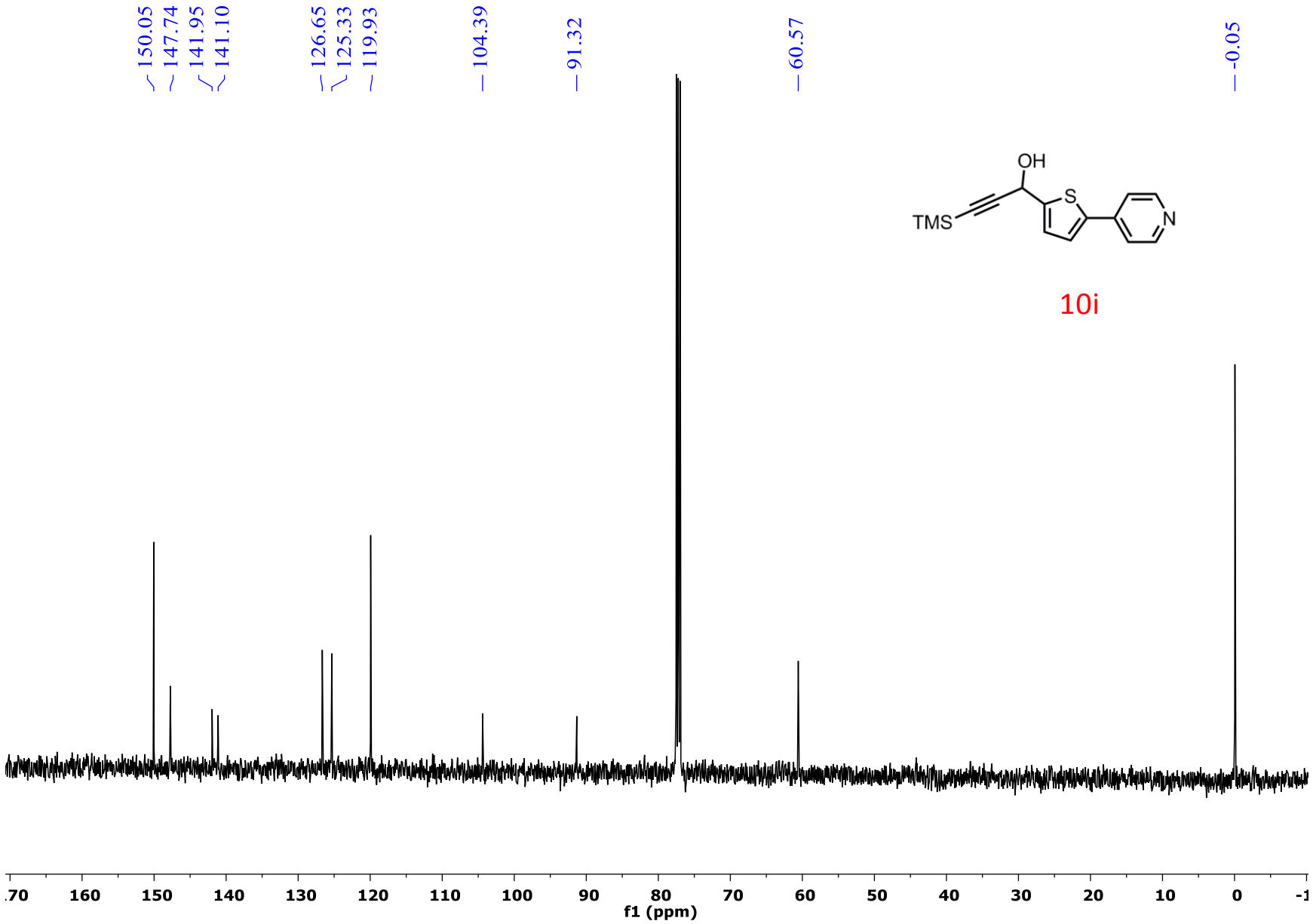
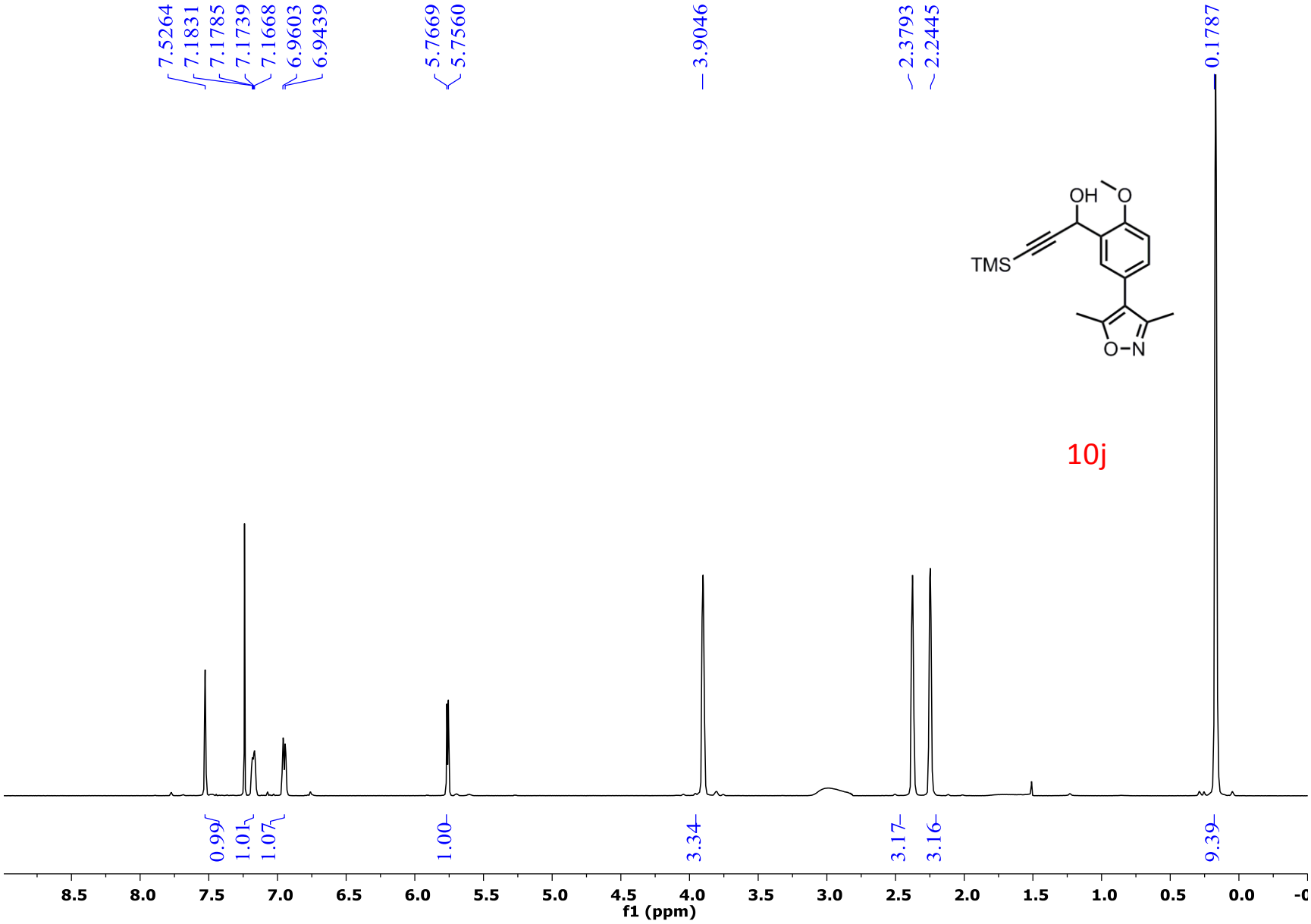
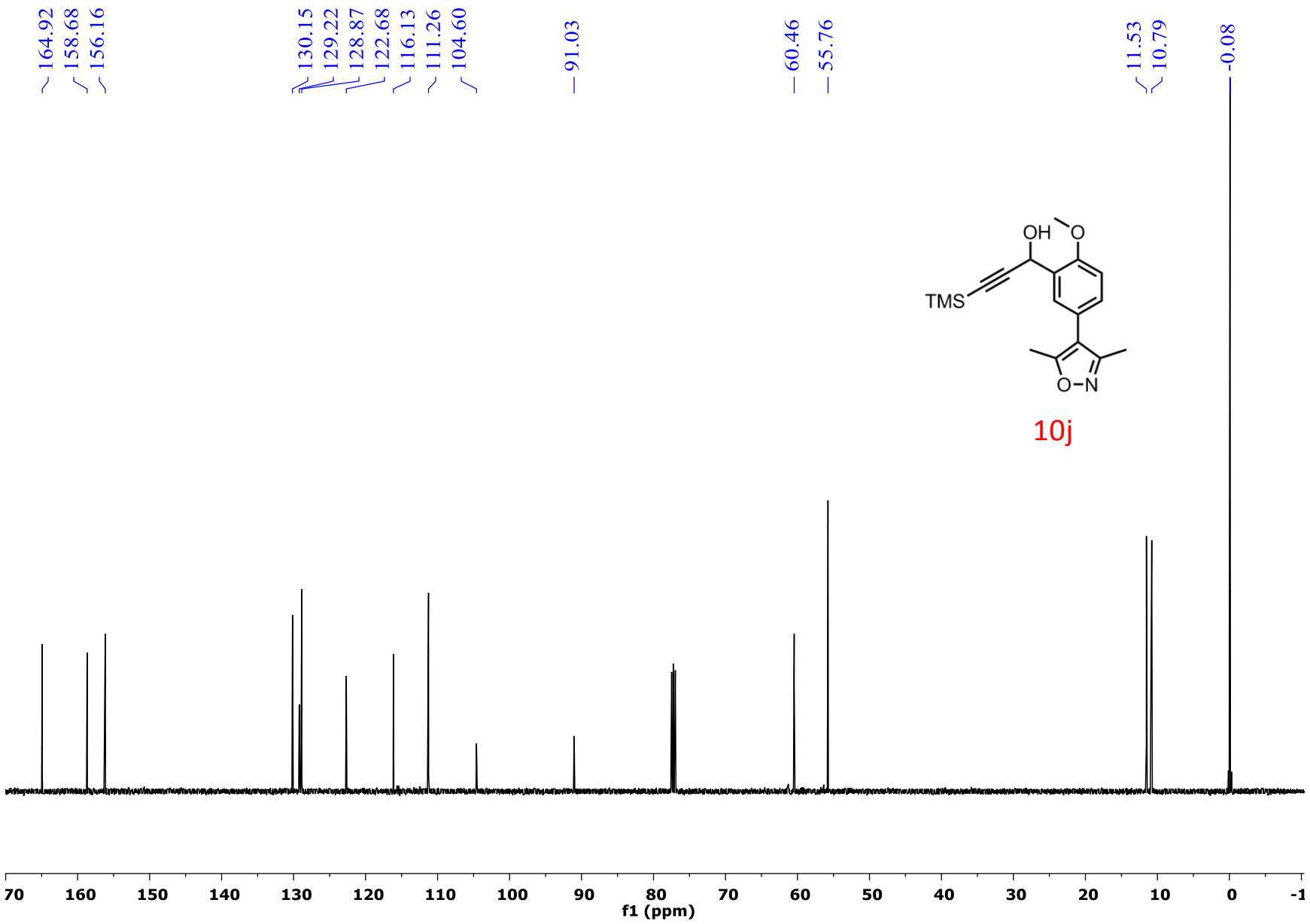
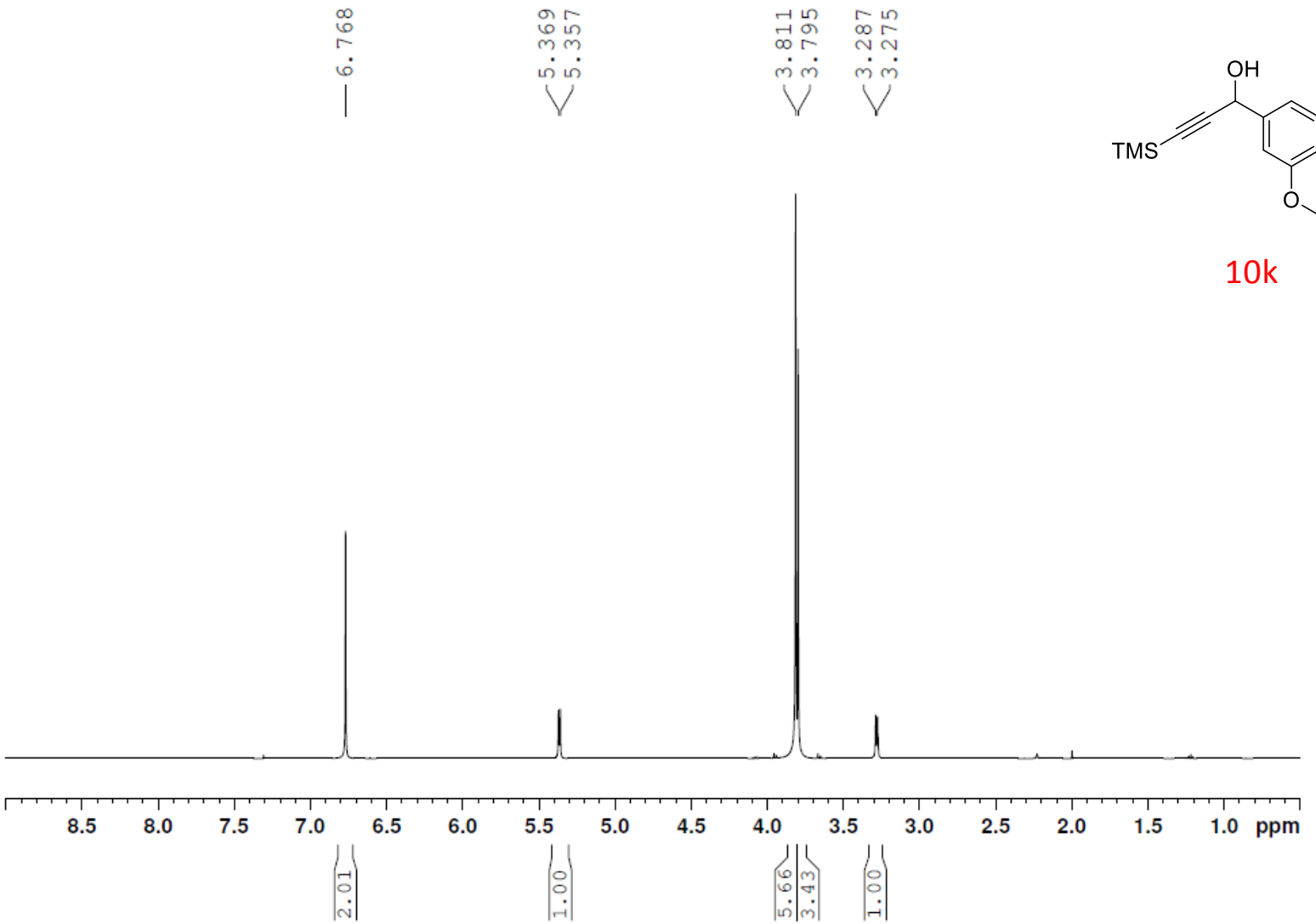
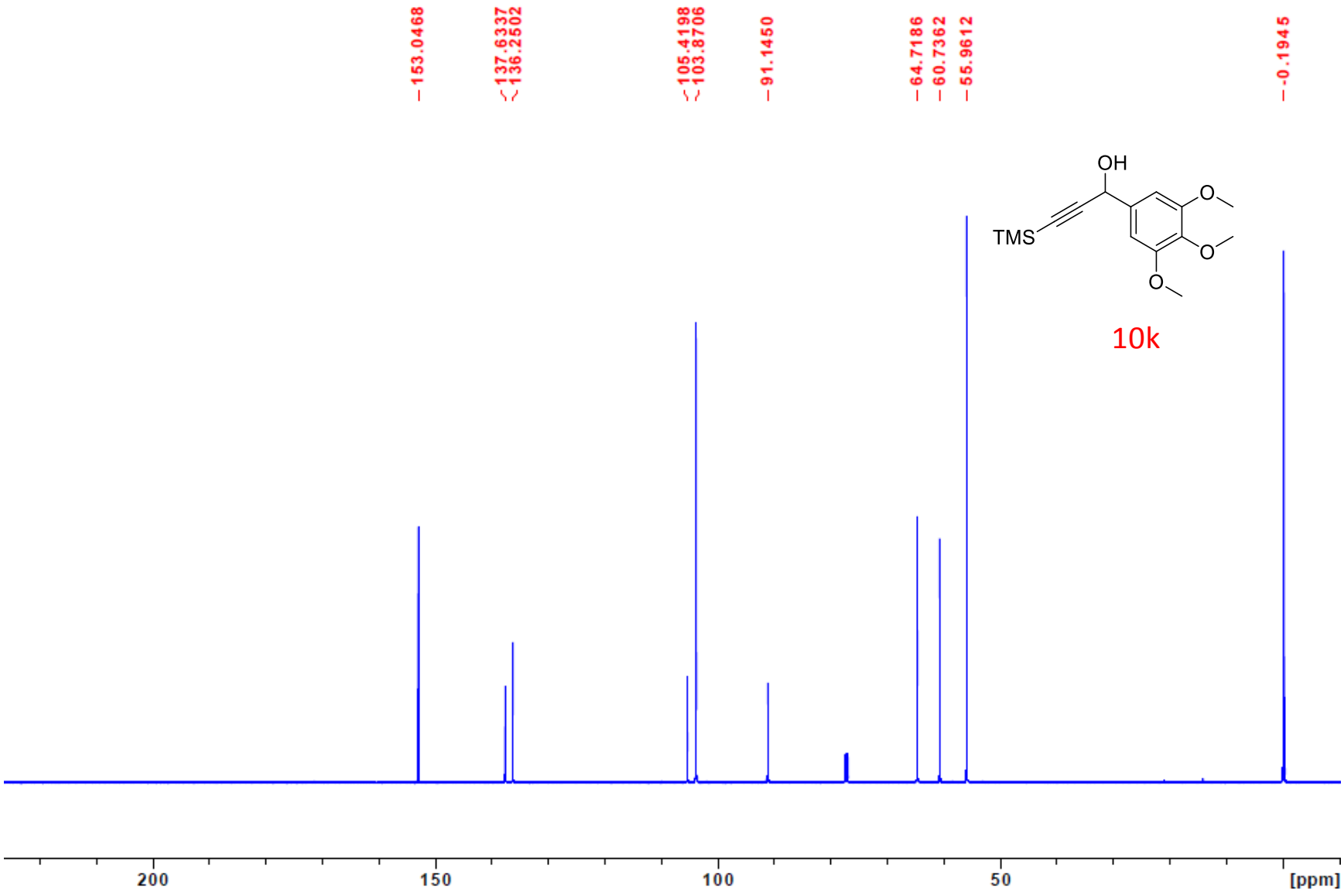
8.4865
7.4155
7.4032
7.3341
7.3266
7.1455
7.1381
5.6535
0.1875
OH
TMS
S
N
10i
2.03
2.07
1.03
1.01
1.00
8.97
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

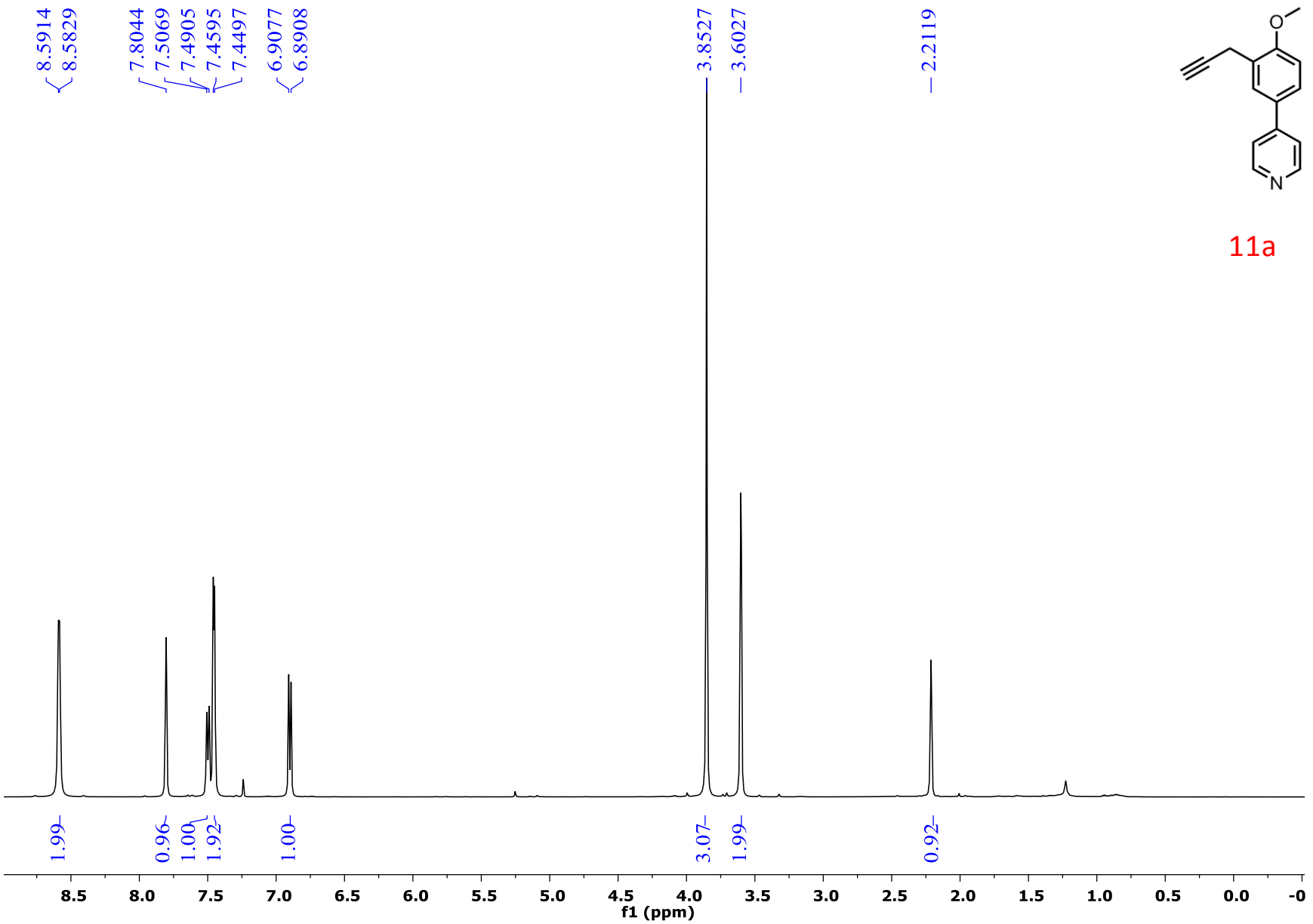

150.05
147.74
141.95
141.10
126.65
125.33
119.93
104.39
91.32
60.57
-0.05
OH
TMS
S
N
10i
f1 (ppm)

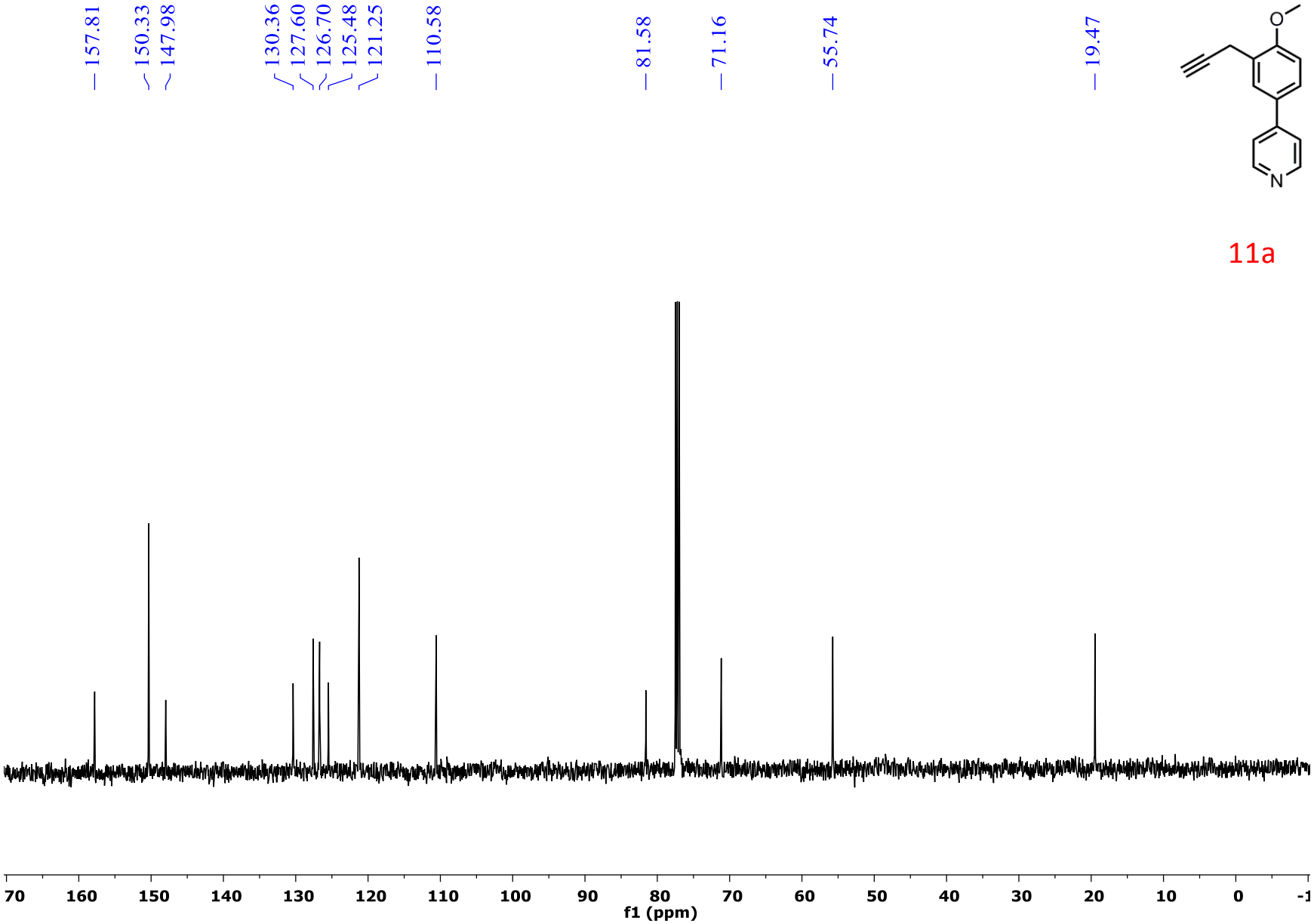

7.5264
7.1831
7.1785
7.1739
7.1668
6.9603
6.9439
5.7669
5.7560
3.9046
2.3793
2.2445
0.1787
OH
O
TMS
O–N
10j
0.99
1.01
1.07
1.00
3.34
3.17
3.16
9.39
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

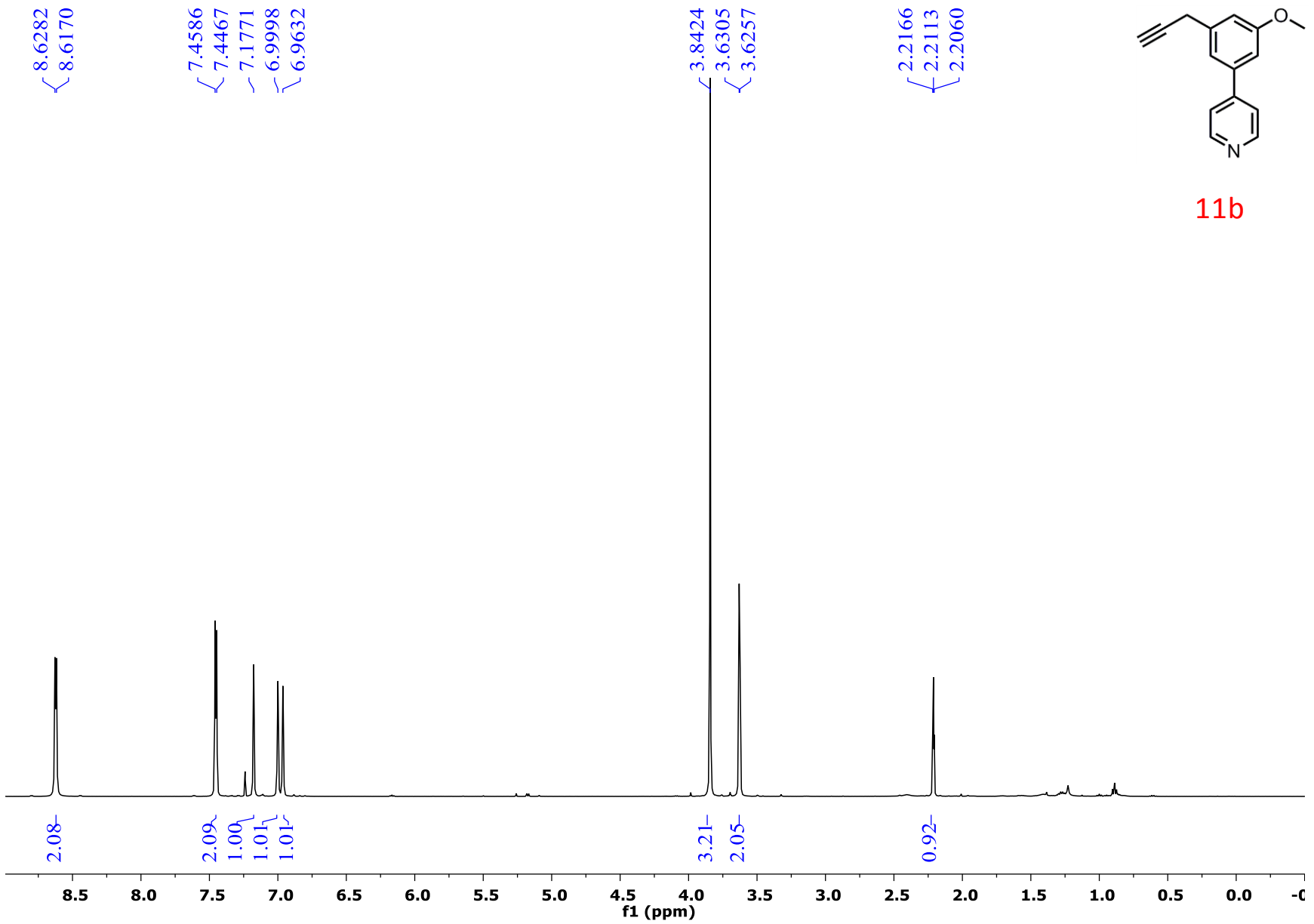

164.92
158.68
156.16
130.15
129.22
128.87
122.68
116.13
111.26
104.60
91.03
60.46
55.76
11.53
10.79
-0.08
OH
O
TMS
O–N
10j
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

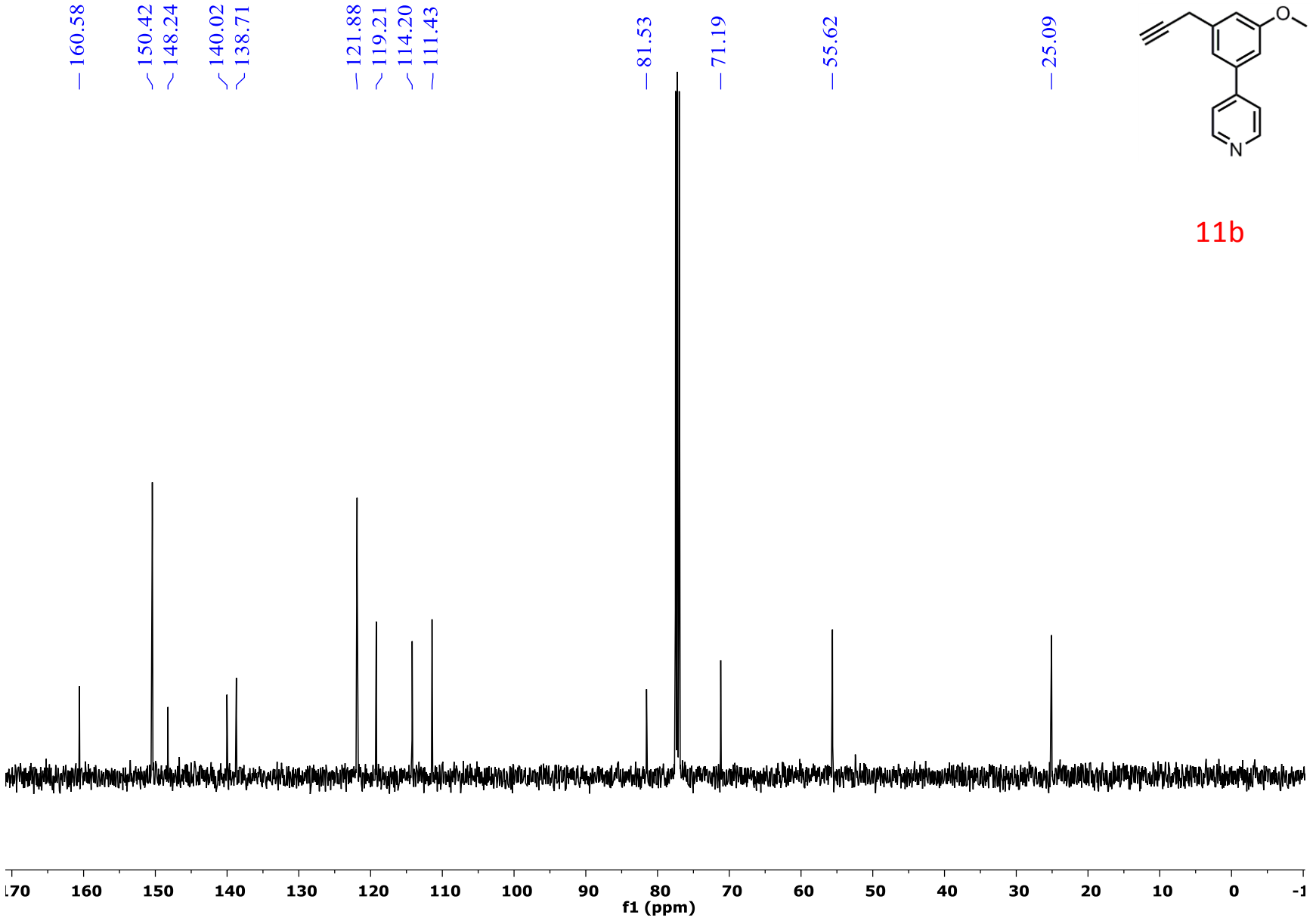

6.768
5.369
5.357
3.811
3.795
3.287
3.275
OH
TMS
O
O
O
10k
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.01
1.00
5.66
3.43
1.00

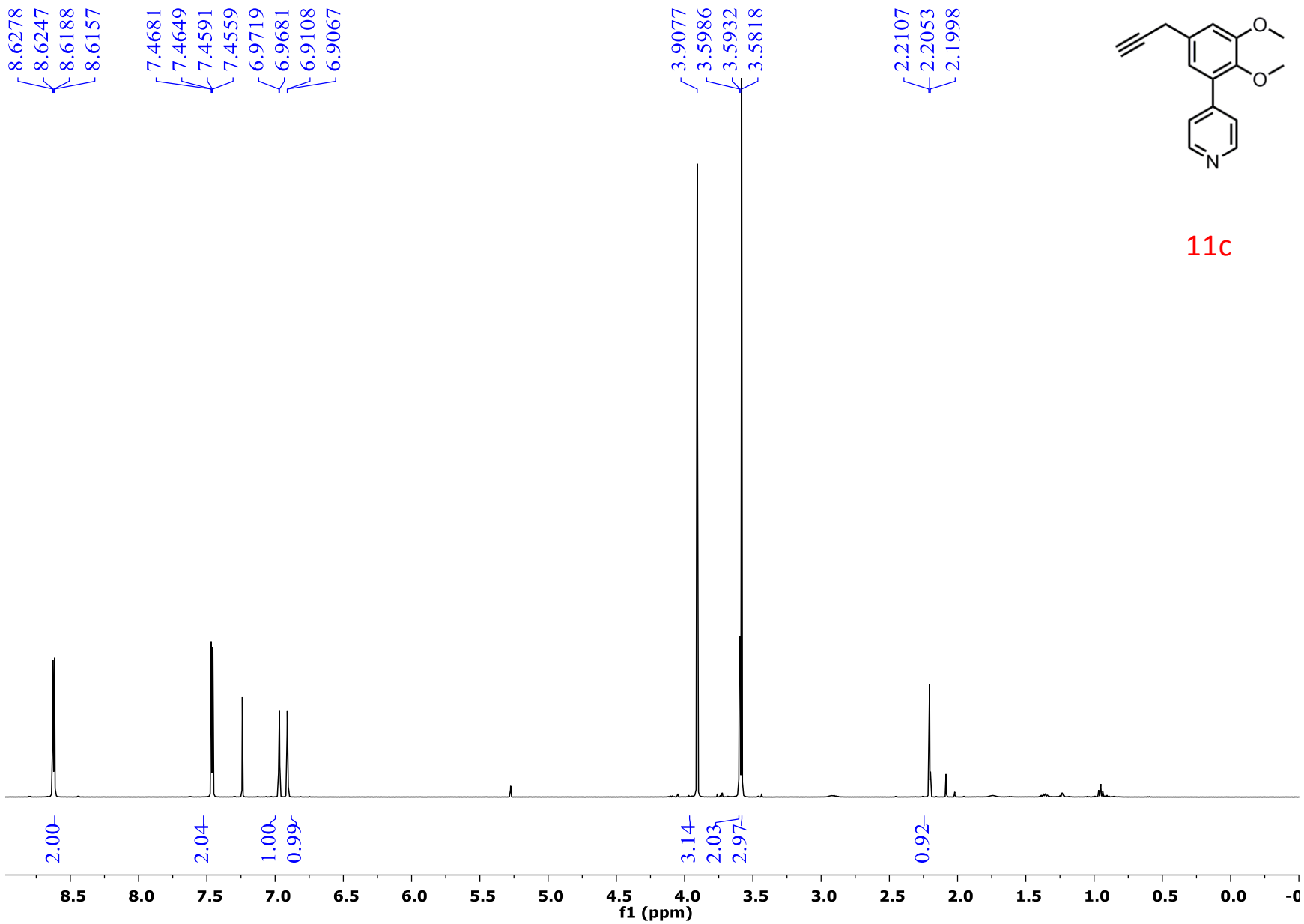

153.0468
137.6337
136.2502
105.4198
103.8706
91.1450
64.7186
60.7362
55.9612
-0.1945
OH
TMS
O
O
O
10k
200
150
100
50
[ppm]

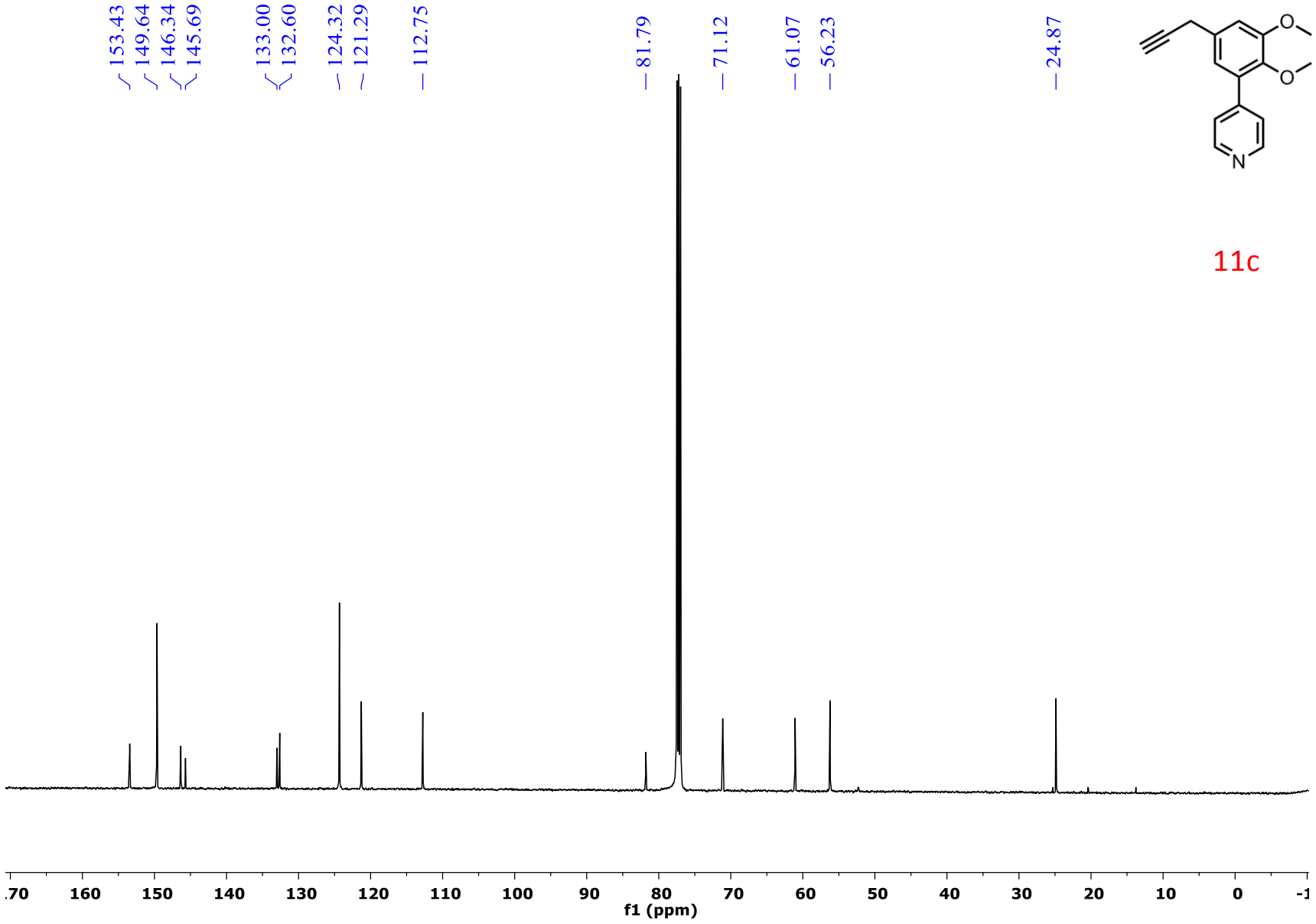

8.5914
8.5829
7.8044
7.5069
7.4905
7.4595
7.4497
6.9077
6.8908
3.8527
3.6027
2.2119
O
N
11a
1.99
0.96
1.00
1.92
1.00
3.07
1.99
0.92
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

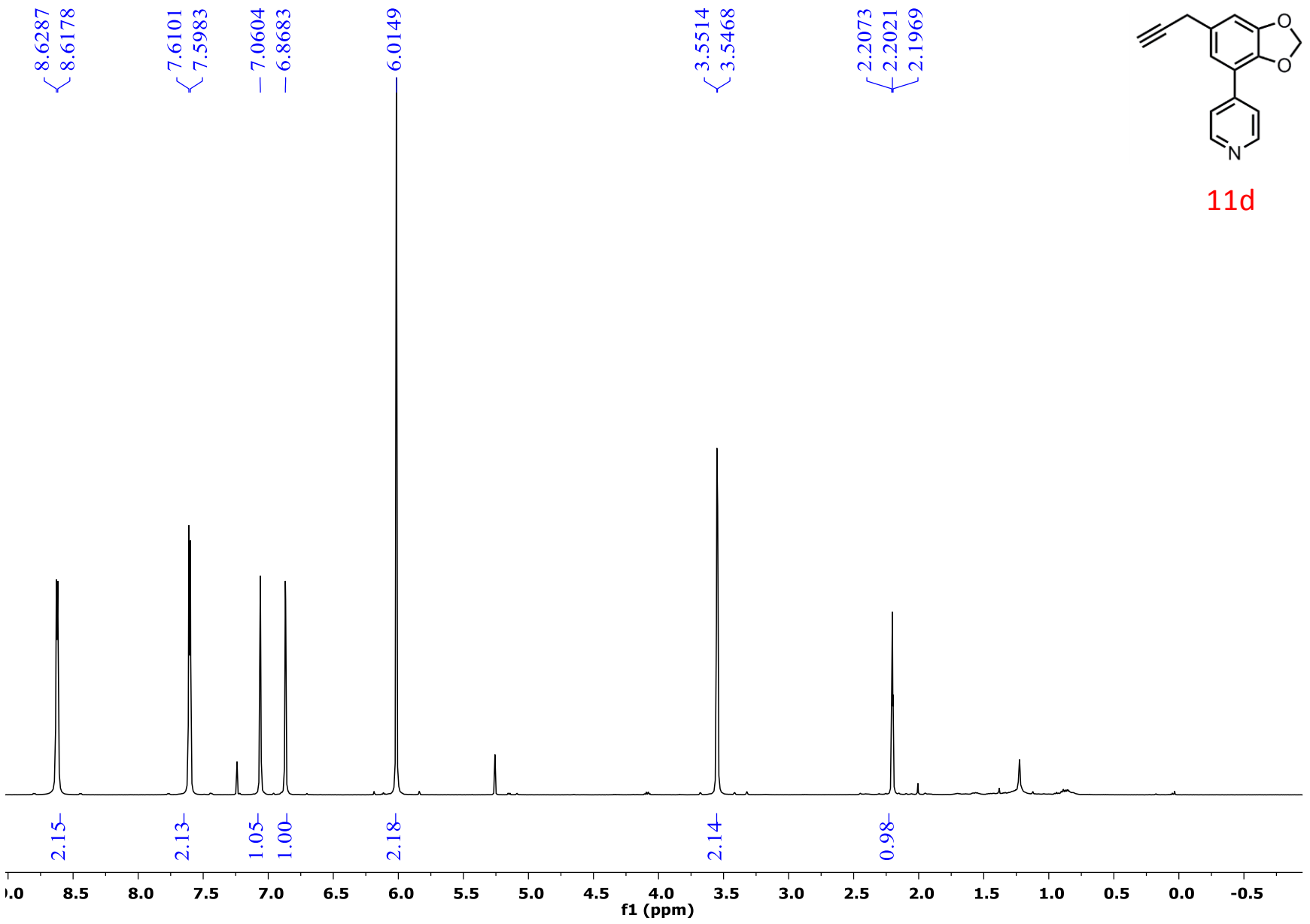

157.81
150.33
147.98
130.36
127.60
126.70
125.48
121.25
110.58
81.58
71.16
55.74
19.47
O
N
11a
70
160
150
140
130
120
110
100
90
80
f1 (ppm)
70
60
50
40
30
20
10
0
-1


8.6282
8.6170
7.4586
7.4467
7.1771
6.9998
6.9632
3.8424
3.6305
3.6257
2.2166
2.2113
2.2060
O
N
11b
2.08
2.09
1.00
1.01
1.01
3.21
2.05
0.92
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

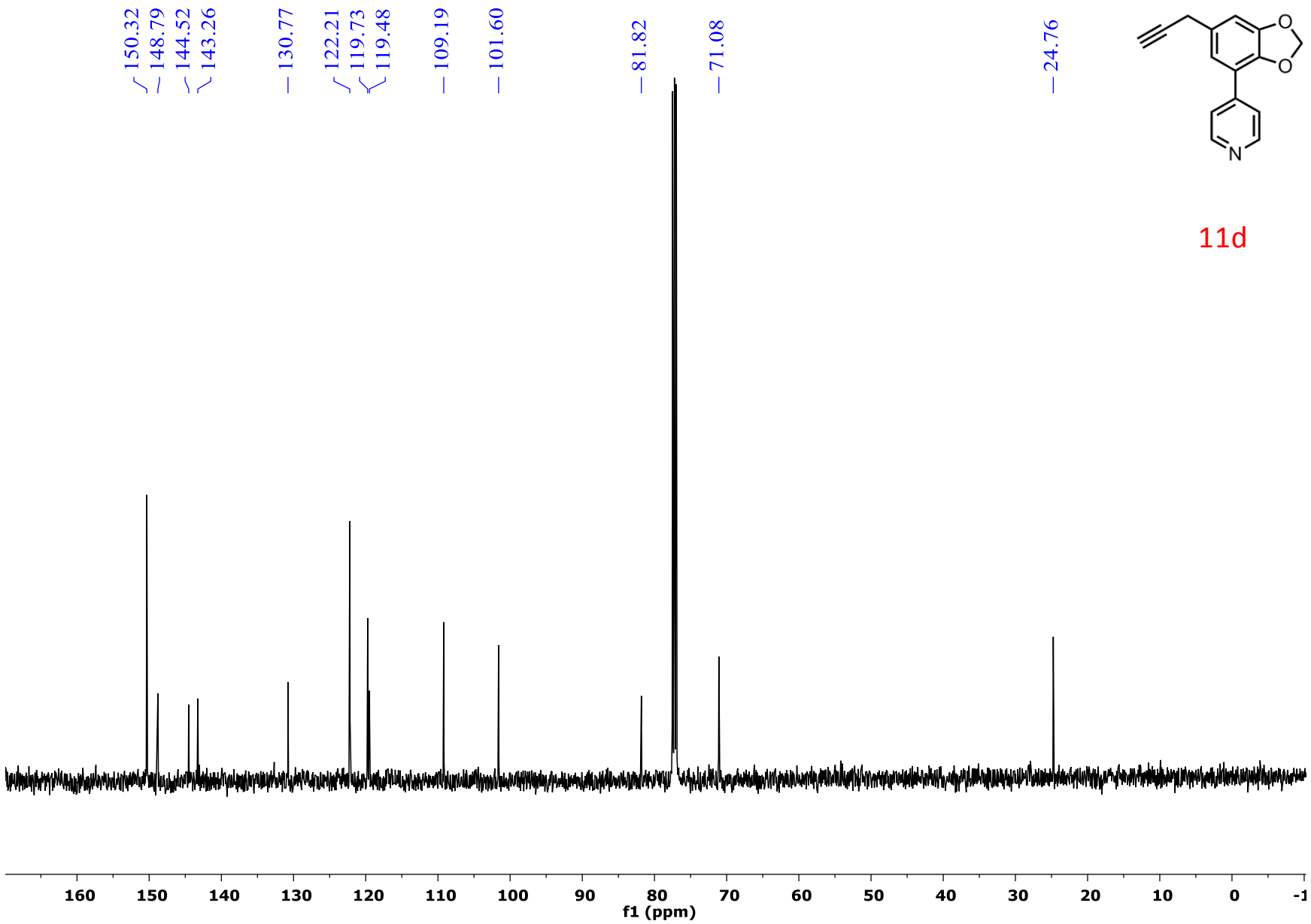

160.58
150.42
148.24
140.02
138.71
121.88
119.21
114.20
111.43
81.53
71.19
55.62
25.09
O
N
11b
f1 (ppm)

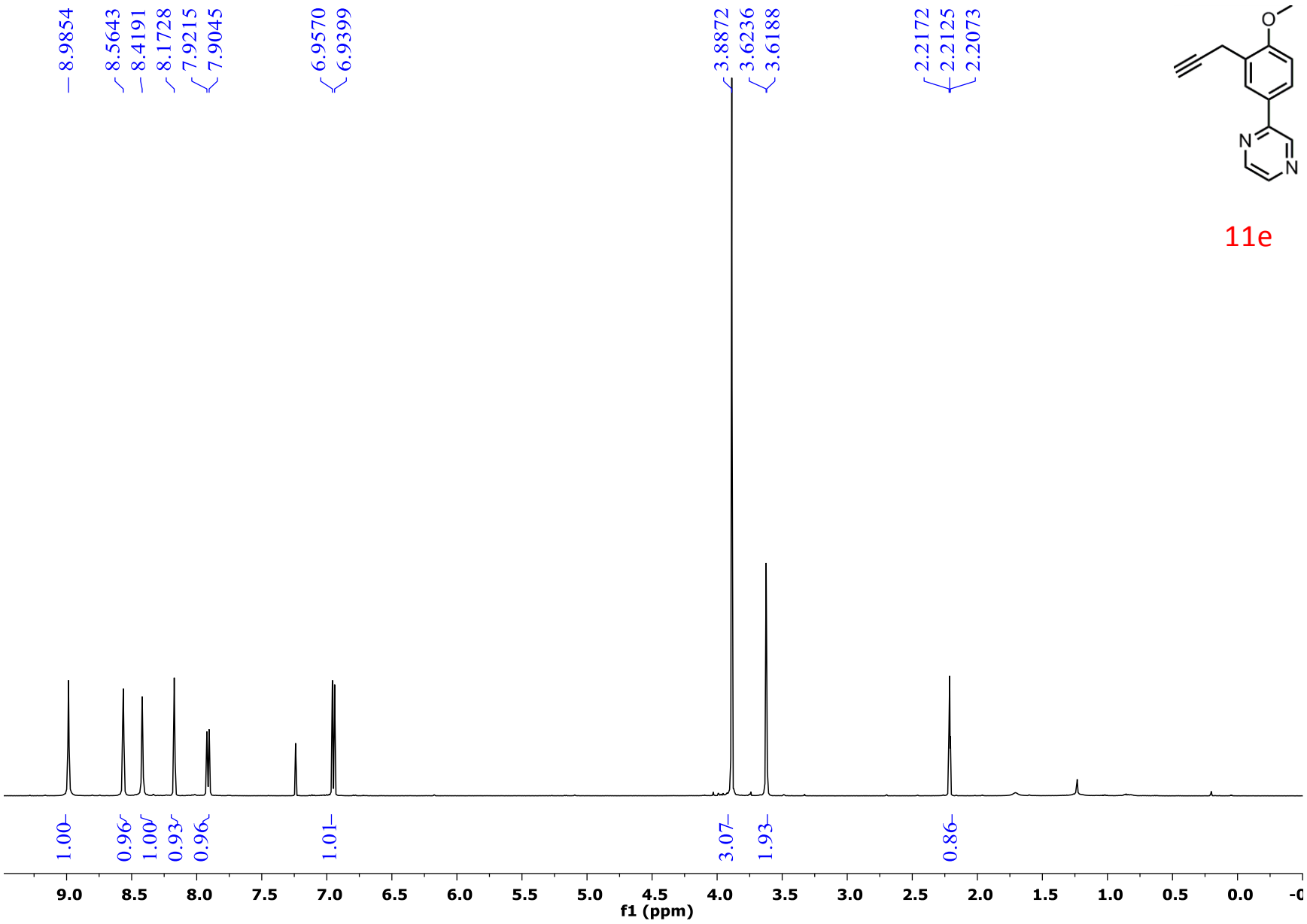

8.6278
8.6247
8.6188
8.6157
7.4681
7.4649
7.4591
7.4559
6.9719
6.9681
6.9108
6.9067
3.9077
3.5986
3.5932
3.5818
2.2107
2.2053
2.1998
O
O
N
11c
2.00
2.04
1.00
0.99
3.14
2.03
2.97
0.92
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


153.43
149.64
146.34
145.69
133.00
132.60
124.32
121.29
112.75
81.79
71.12
61.07
56.23
24.87
O
O
N
11c
f1 (ppm)


8.6287
8.6178
7.6101
7.5983
7.0604
6.8683
6.0149
3.5514
3.5468
2.2073
2.2021
2.1969
2.15
2.13
1.05
1.00
2.18
2.14
0.98
f1 (ppm)

11d


150.32
148.79
144.52
143.26
130.77
122.21
119.73
119.48
109.19
101.60
81.82
71.08
24.76
O
O
N
11d
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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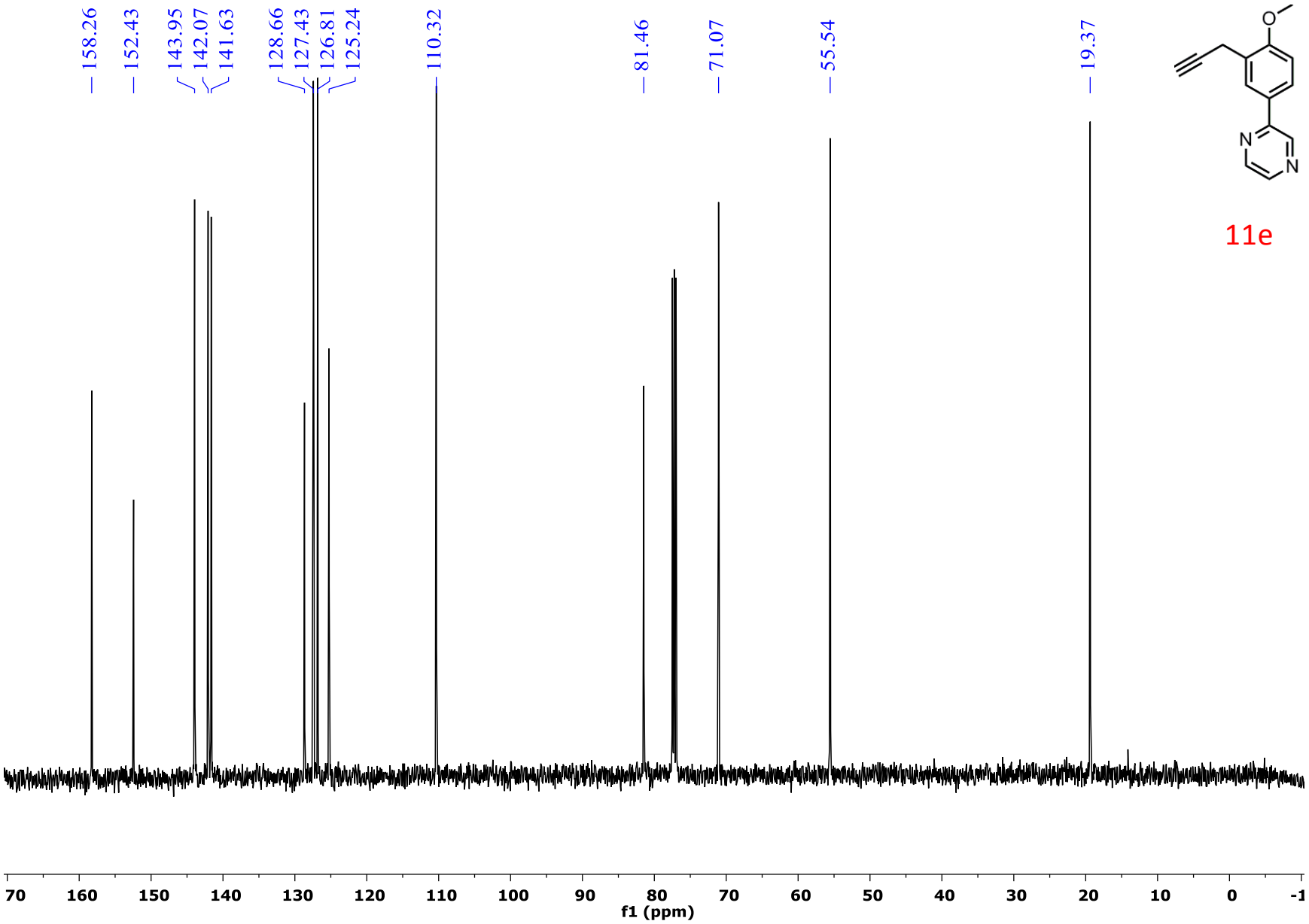
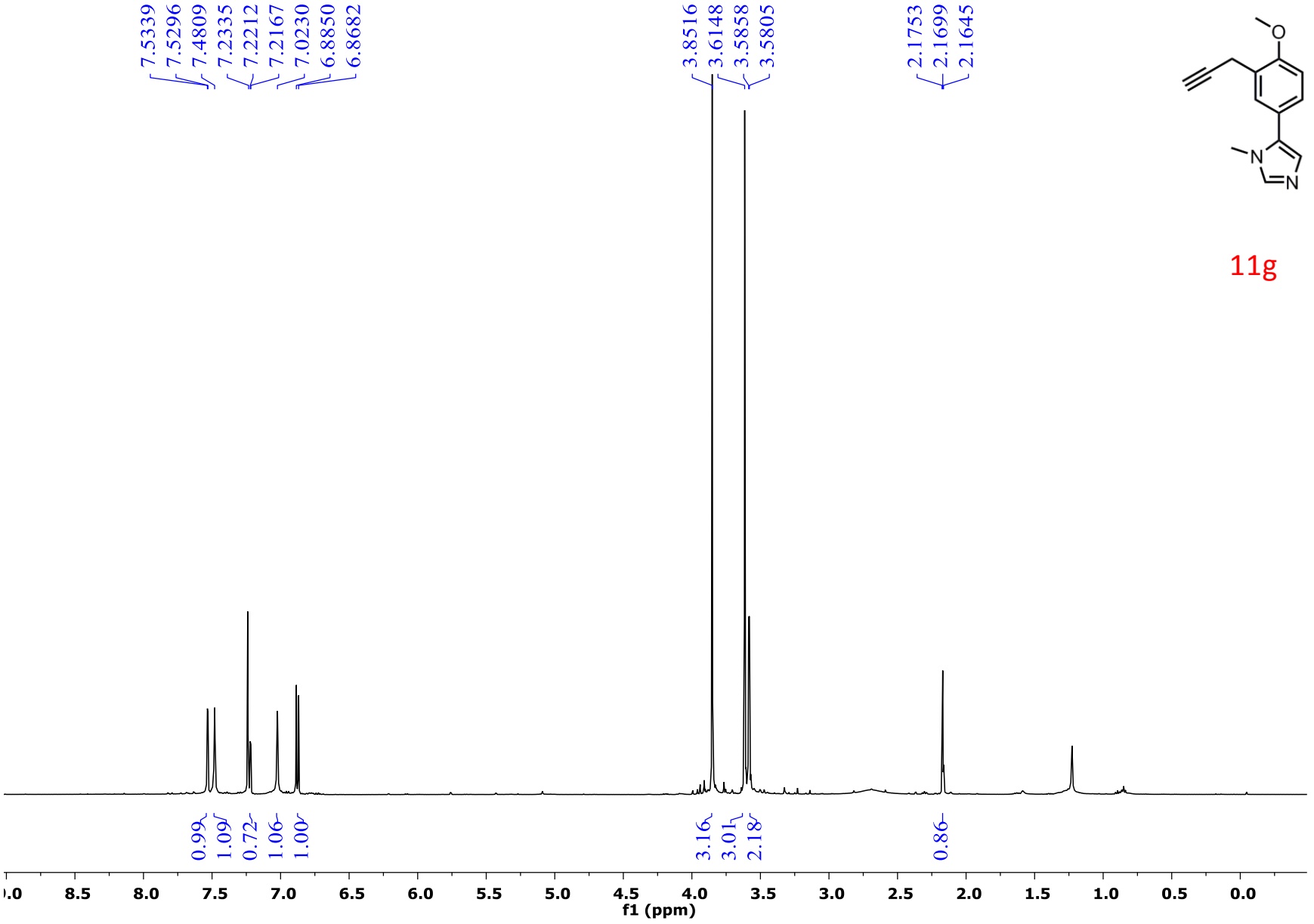
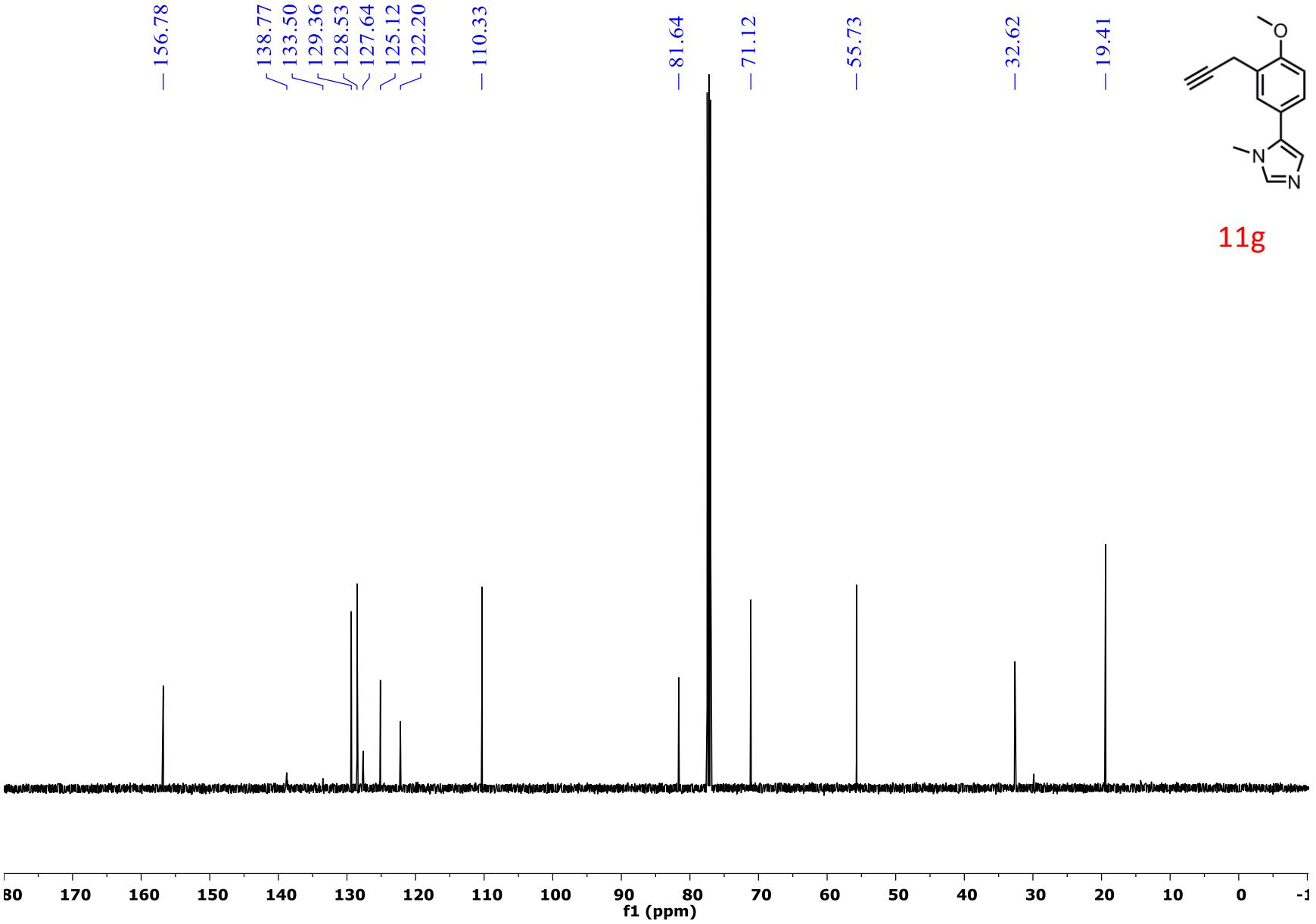
8.4191
8.1728
7.9215
7.9045
6.9570
6.9399
3.8872
3.6236
3.6188
2.2172
2.2125
2.2073
1.00
0.96
1.00
0.93
0.96
1.01
3.07
1.93
0.86
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
N
N

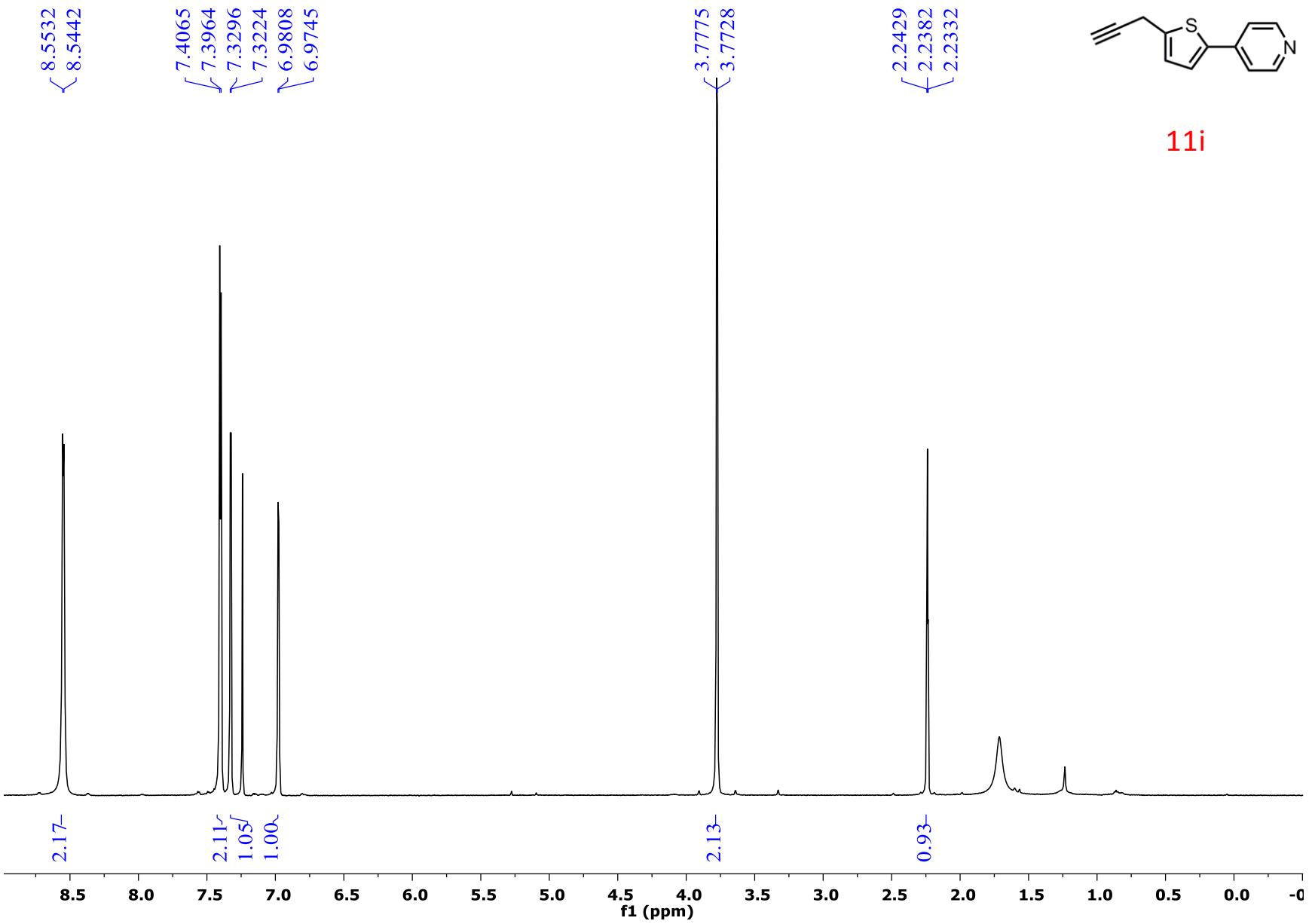
11e


158.26
152.43
143.95
142.07
141.63
128.66
127.43
126.81
125.24
110.32
81.46
71.07
55.54
19.37
O
N
N
11e
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.5339
7.5296
7.4809
7.2335
7.2212
7.2167
7.0230
6.8850
6.8682
3.8516
3.6148
3.5858
3.5805
2.1753
2.1699
2.1645
0.99
1.09
0.72
1.06
1.00
3.16
3.01
2.18
0.86
f1 (ppm)

11g


156.78
138.77
133.50
129.36
128.53
127.64
125.12
122.20
110.33
81.64
71.12
55.73
32.62
19.41
O
N
N
11g
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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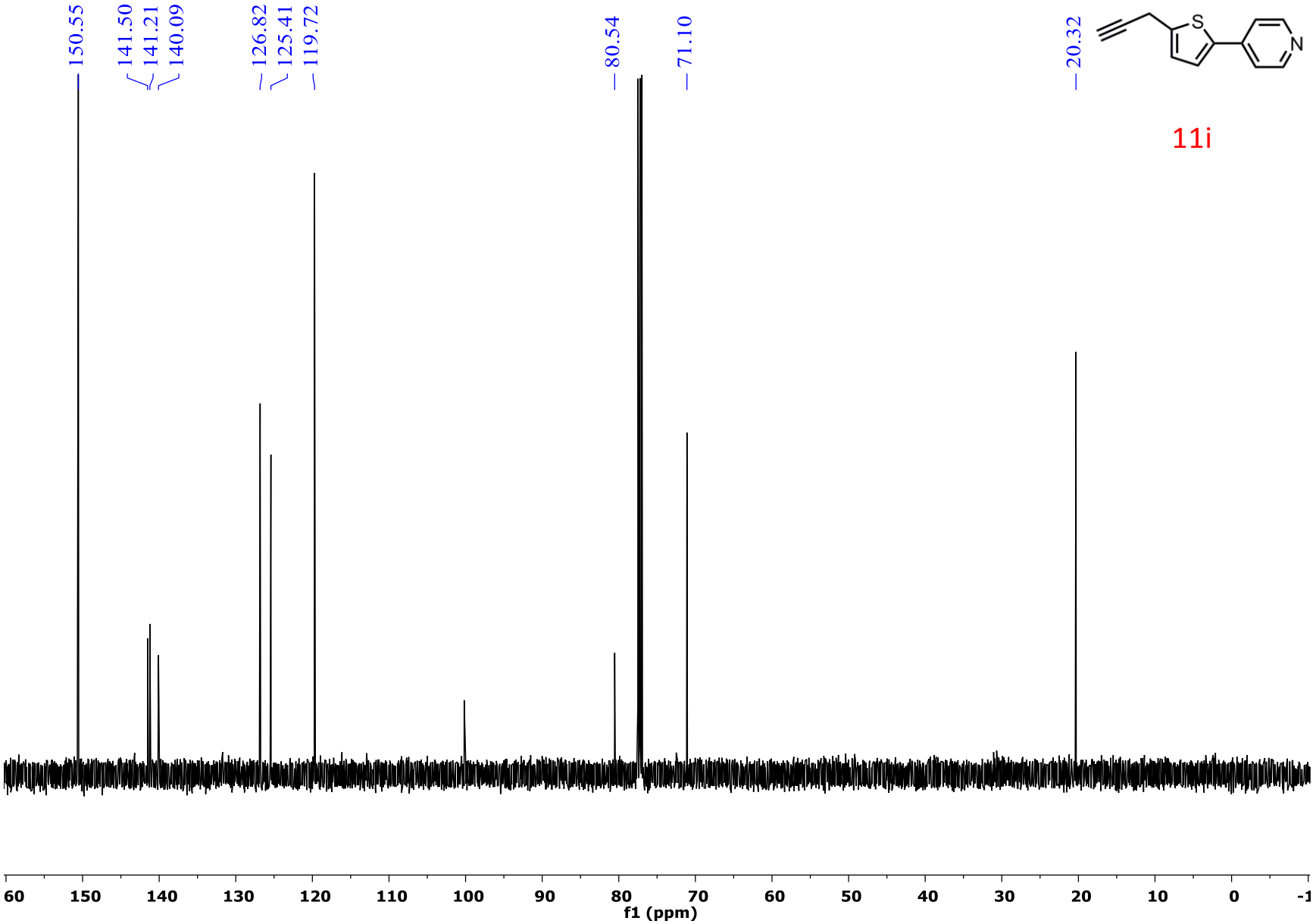
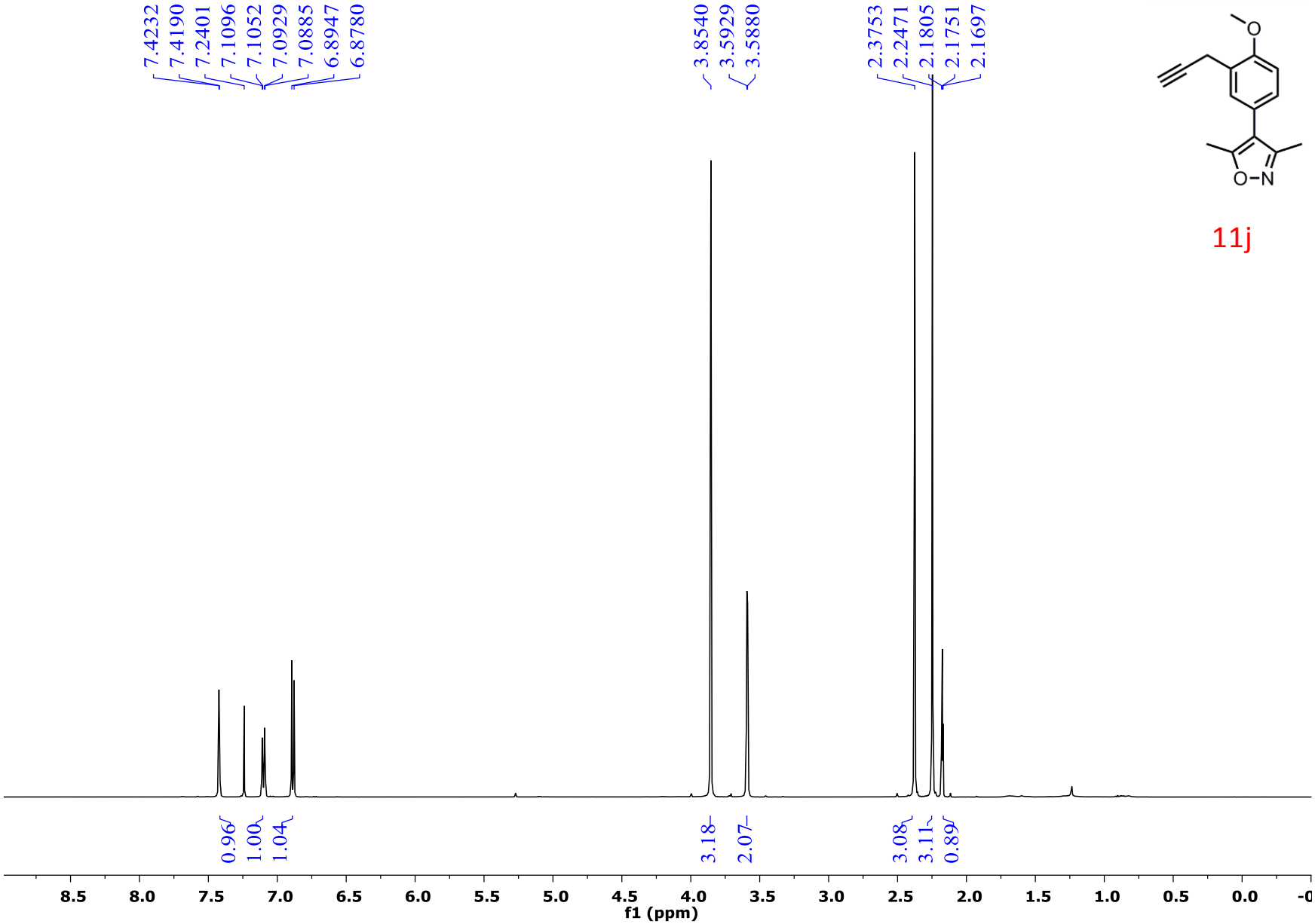
8.5442
7.4065
7.3964
7.3296
7.3224
6.9808
6.9745
3.7775
3.7728
2.2429
2.2382
2.2332
S
N
11i
2.17
2.11
1.05
1.00
2.13
0.93
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


150.55
141.50
141.21
140.09
126.82
125.41
119.72
80.54
71.10
20.32
S
N
11i
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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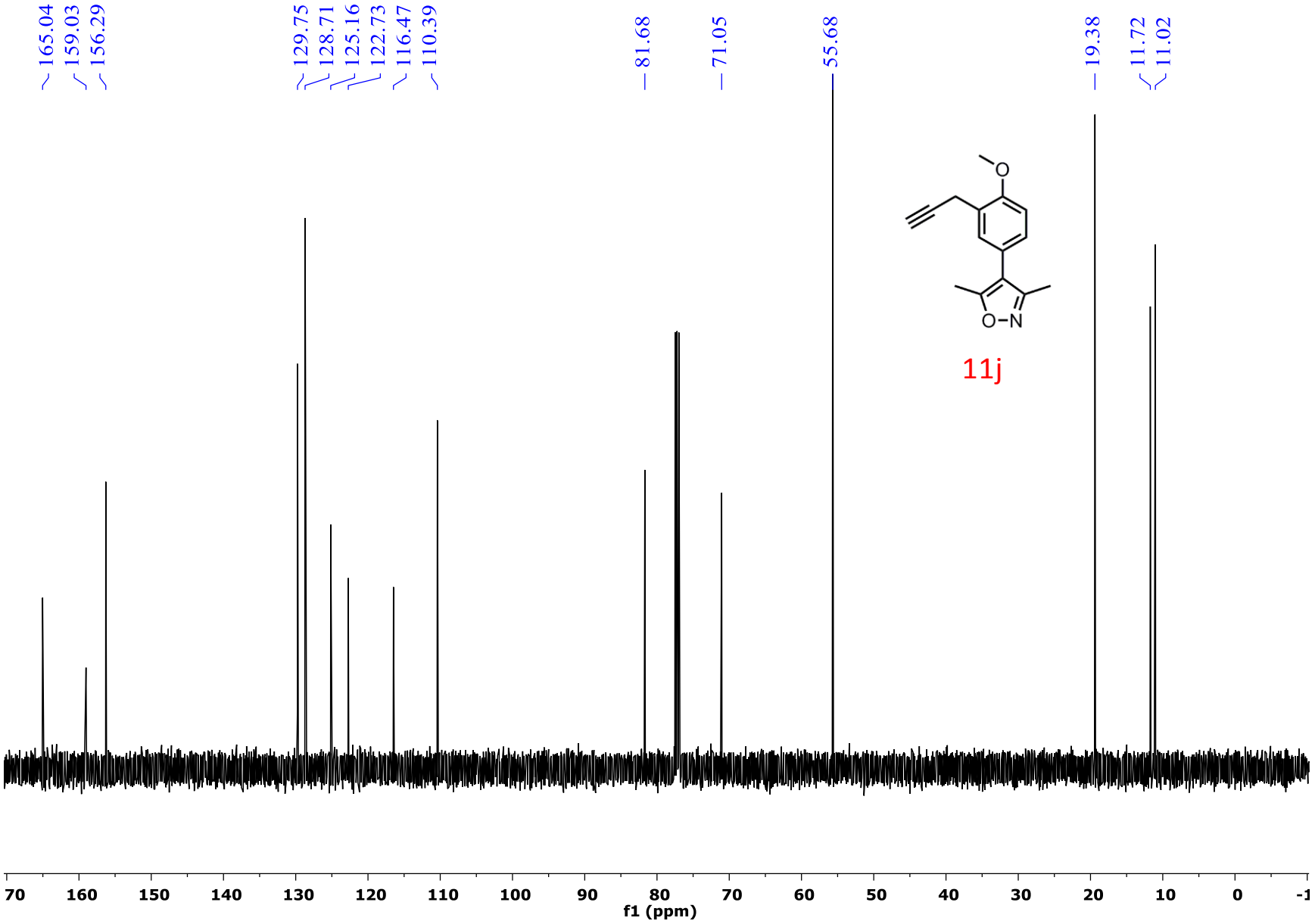
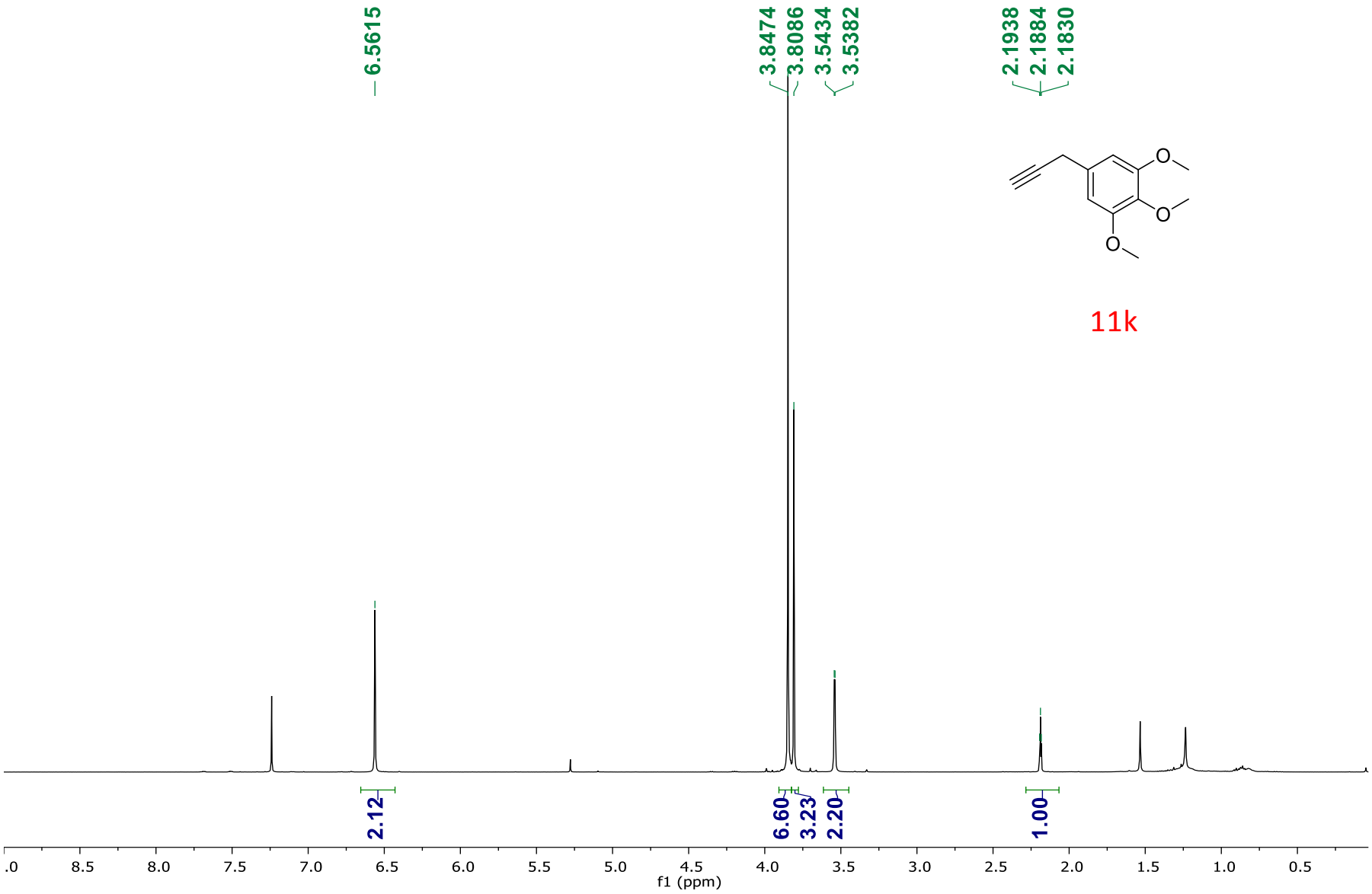
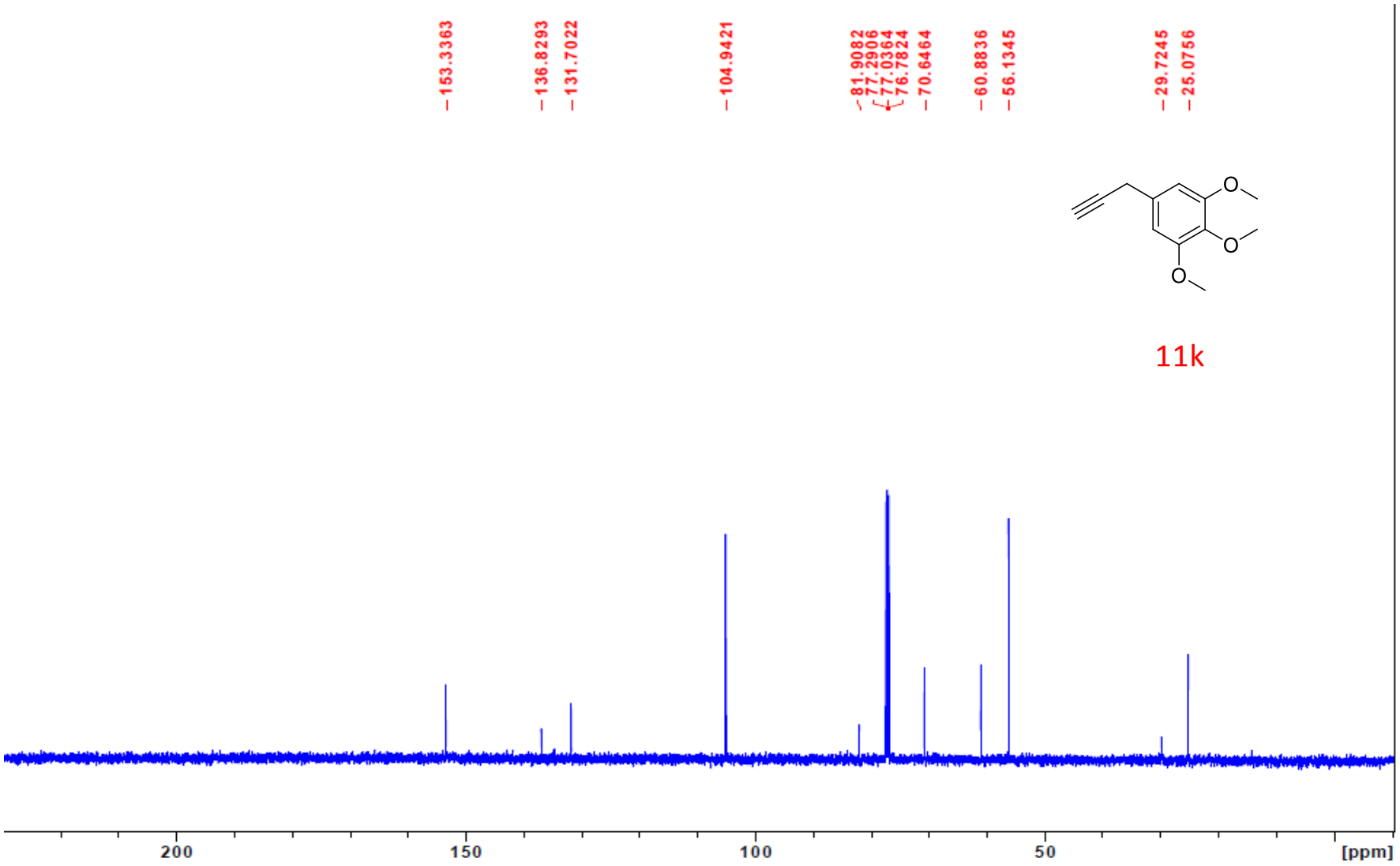
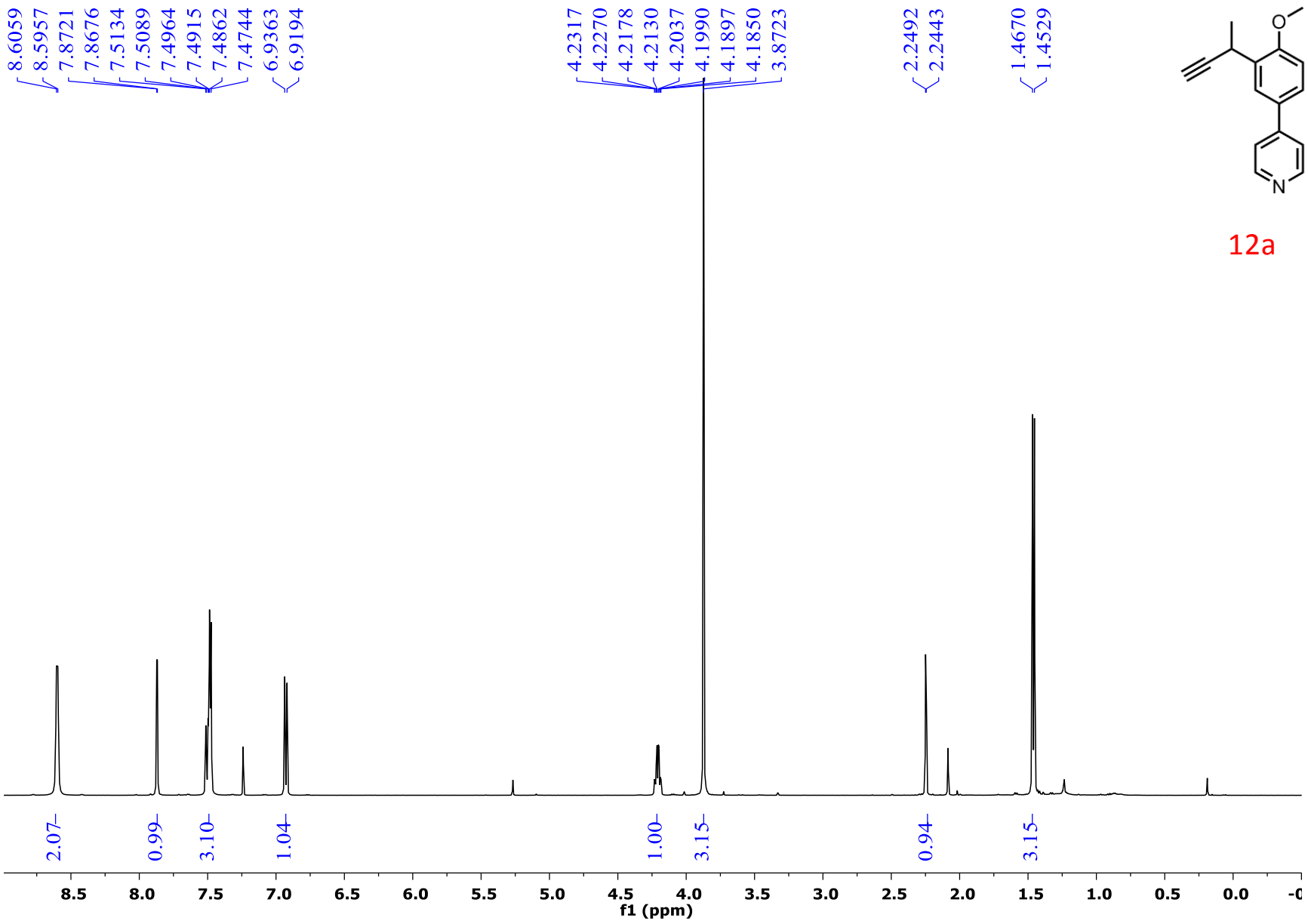
7.2401
7.1096
7.1052
7.0929
7.0885
6.8947
6.8780
3.8540
3.5929
3.5880
2.3753
2.2471
2.1805
2.1751
2.1697
0.96
1.00
1.04
3.18
2.07
3.08
3.11
0.89
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
O-N

11j


165.04
159.03
156.29
129.75
128.71
125.16
122.73
116.47
110.39
81.68
71.05
55.68
19.38
11.72
11.02
O
O–N
11j
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


6.5615
3.8474
3.8086
3.5434
3.5382
2.1938
2.1884
2.1830
O
O
O
11k
2.12
6.60
3.23
2.20
1.00
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


153.3363
136.8293
131.7022
104.9421
81.9082
77.2906
77.0364
76.7824
70.6464
60.8836
56.1345
29.7245
25.0756
O
O
O
11k
200
150
100
50
[ppm]


8.6059
8.5957
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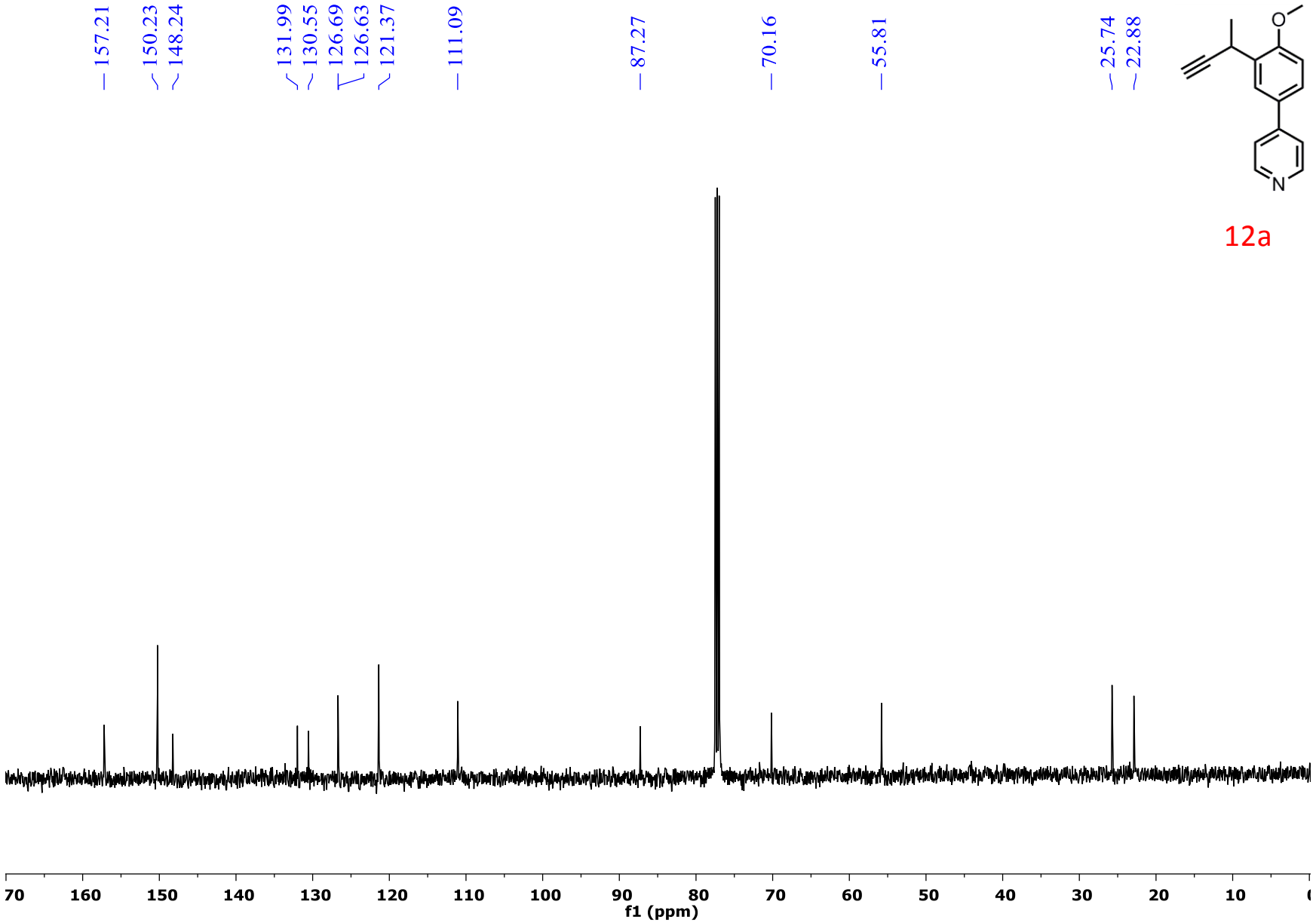
7.8676
7.5134
7.5089
7.4964
7.4915
7.4862
7.4744
6.9363
6.9194
4.2317
4.2270
4.2178
4.2130
4.2037
4.1990
4.1897
4.1850
3.8723
2.2492
2.2443
1.4670
1.4529
O
N
12a
2.07
0.99
3.10
1.04
1.00
3.15
0.94
3.15
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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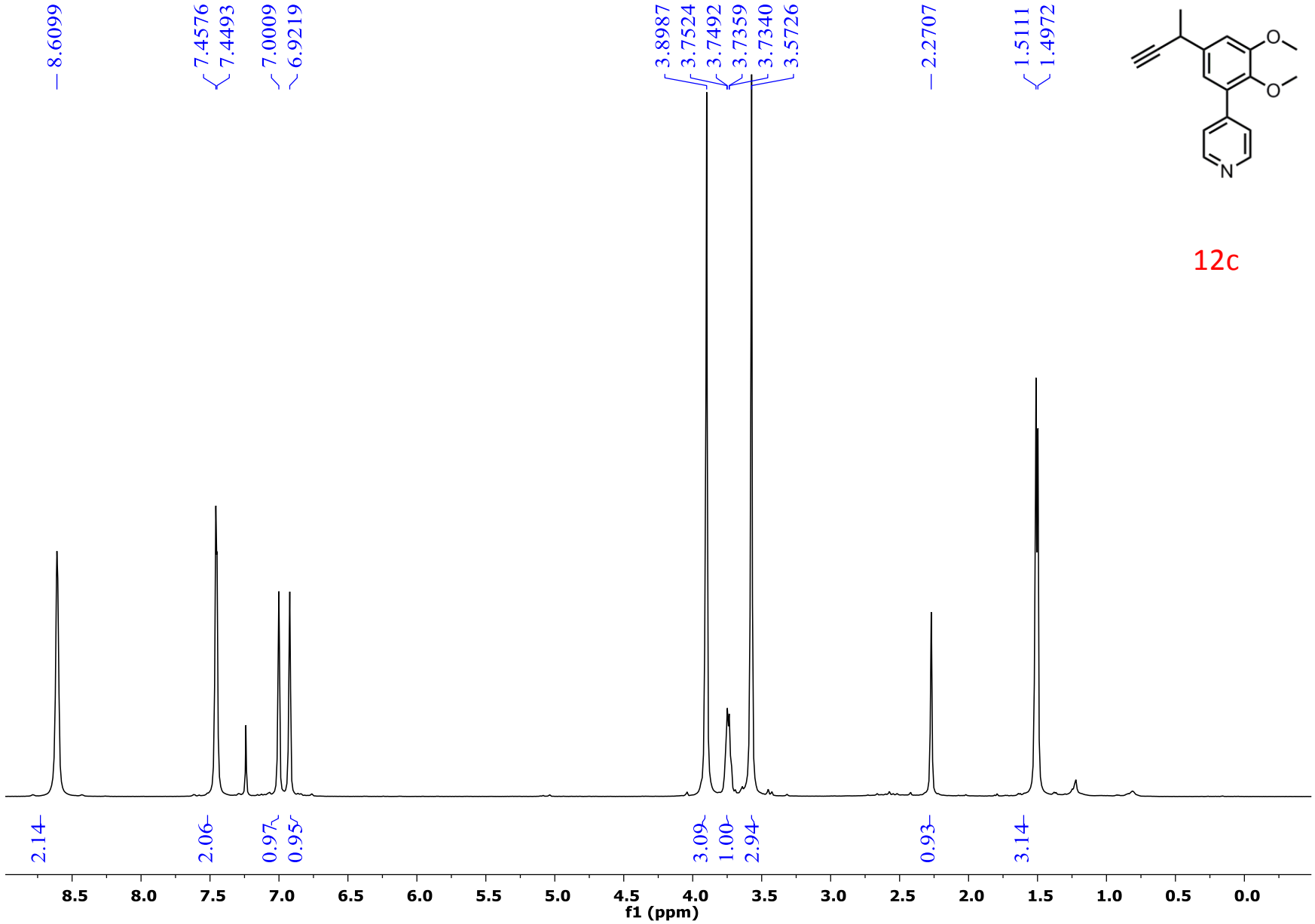
150.23
148.24
131.99
130.55
126.69
126.63
121.37
111.09
87.27
70.16
55.81
25.74
22.88
O
N
12a
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.4493
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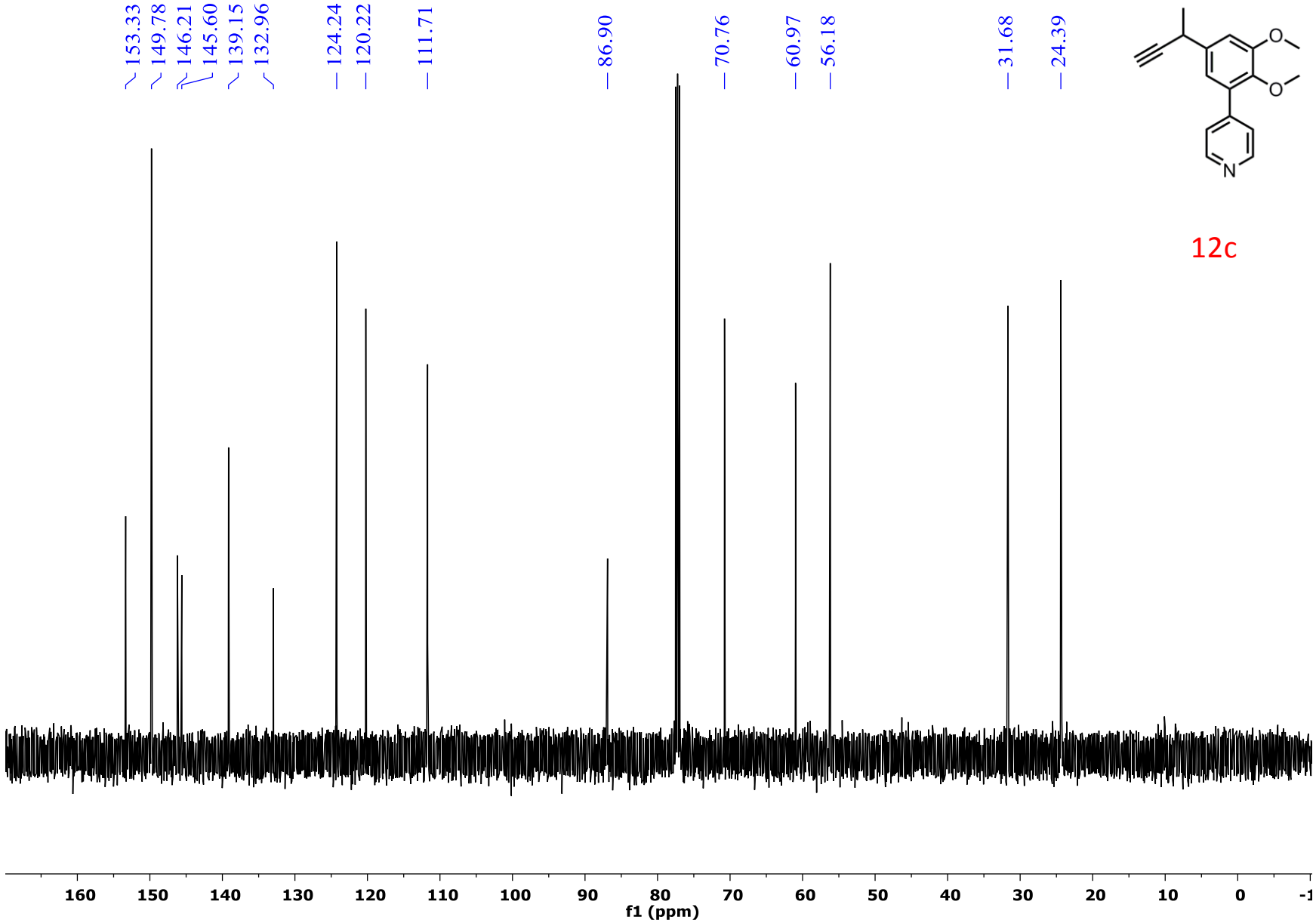
3.7524
3.7492
3.7359
3.7340
3.5726
2.2707
1.5111
1.4972
2.14
2.06
0.97
0.95
3.09
1.00
2.94
0.93
3.14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
O
O
N

12c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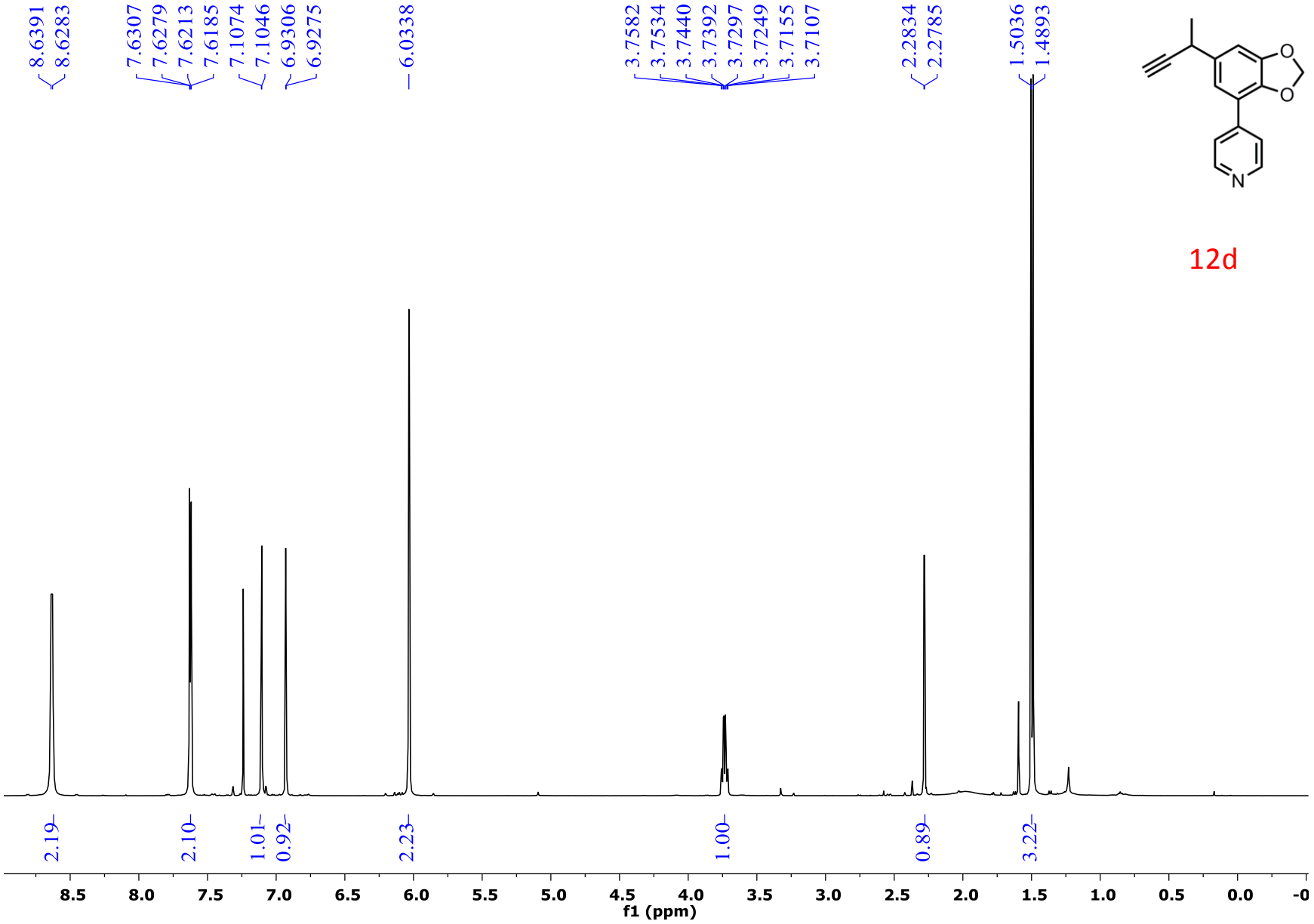
145.60
139.15
132.96
124.24
120.22
111.71
86.90
70.76
60.97
56.18
31.68
24.39
O
O
N
12c
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.6213
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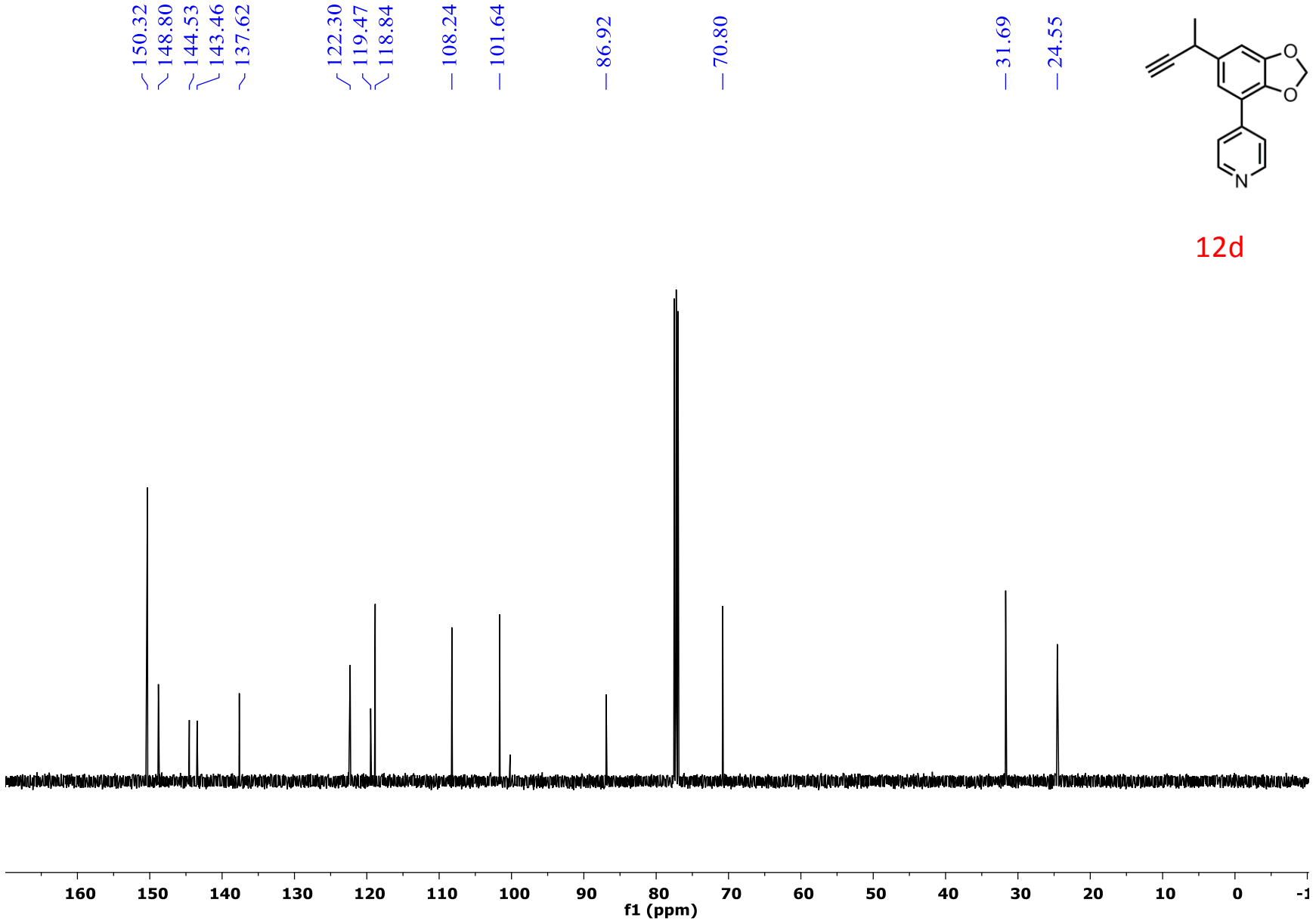
7.1074
7.1046
6.9306
6.9275
6.0338
3.7582
3.7534
3.7440
3.7392
3.7297
3.7249
3.7155
3.7107
2.2834
2.2785
1.5036
1.4893
2.19
2.10
1.01
0.92
2.23
1.00
0.89
3.22
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)
O
O
N

12d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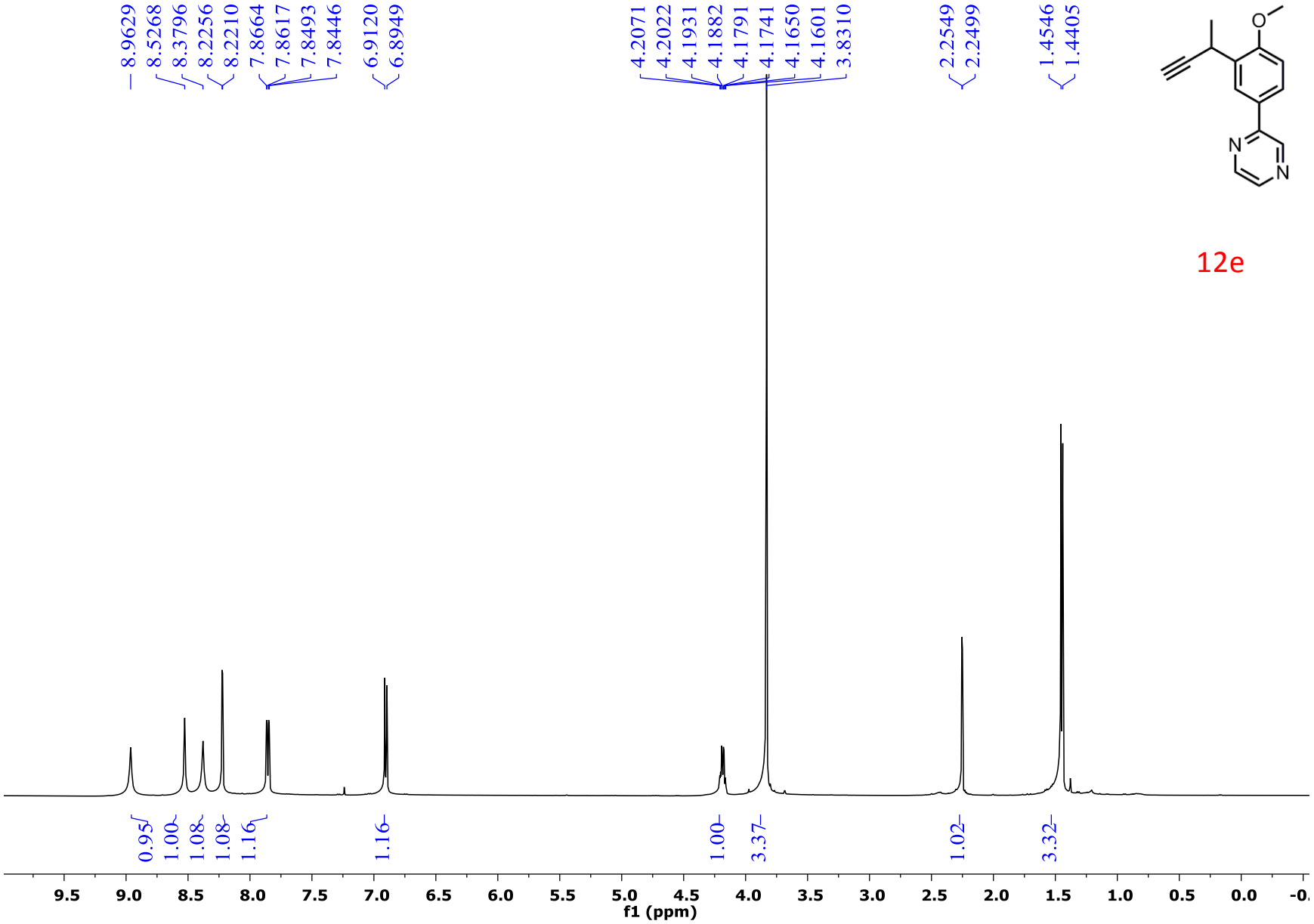
148.80
144.53
143.46
137.62
122.30
119.47
118.84
108.24
101.64
86.92
70.80
31.69
24.55
O
O
N
12d
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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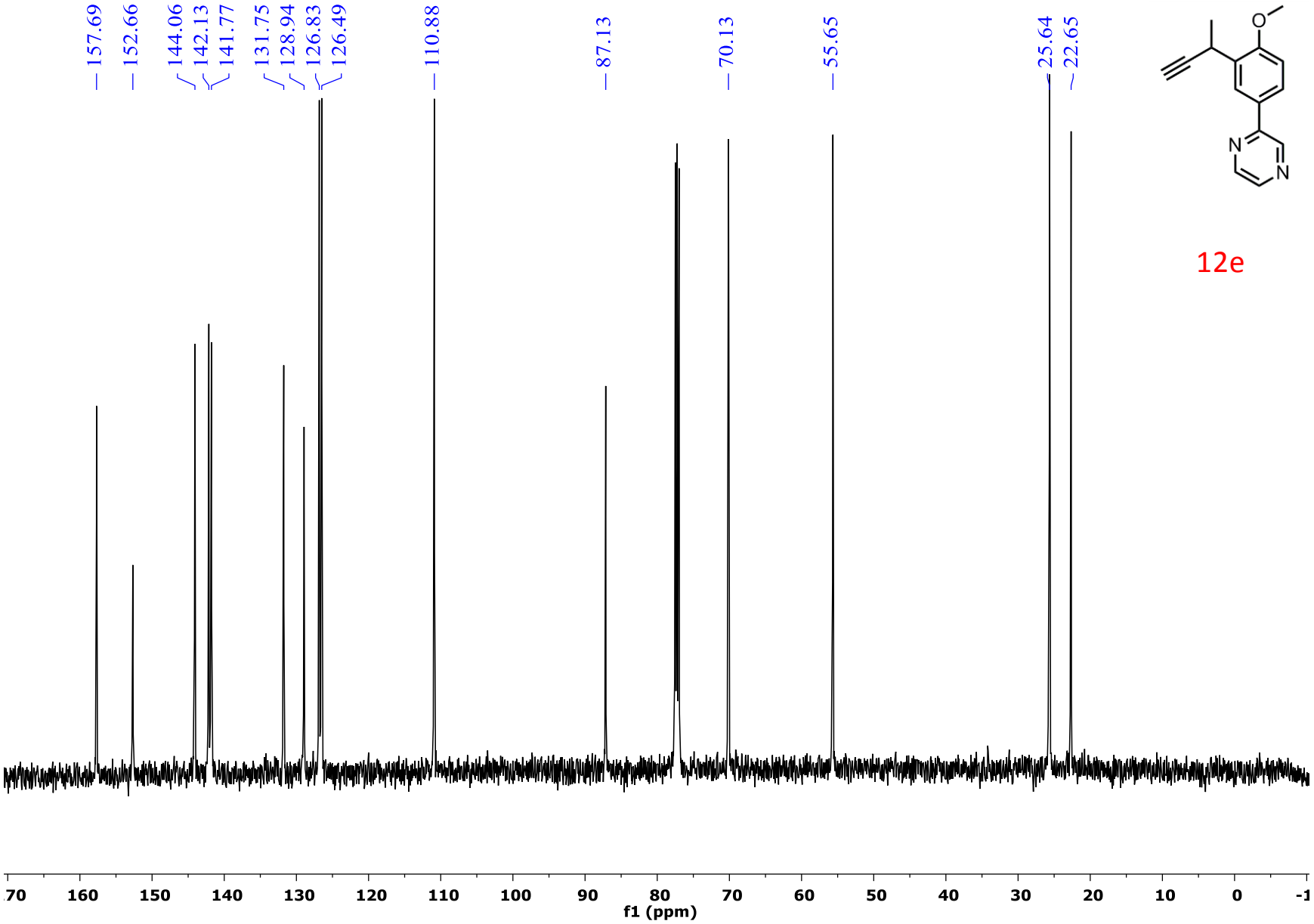
8.3796
8.2256
8.2210
7.8664
7.8617
7.8493
7.8446
6.9120
6.8949
4.2071
4.2022
4.1931
4.1882
4.1791
4.1741
4.1650
4.1601
3.8310
2.2549
2.2499
1.4546
1.4405
O
N
N
12e
0.95
1.00
1.08
1.08
1.16
1.16
1.00
3.37
1.02
3.32
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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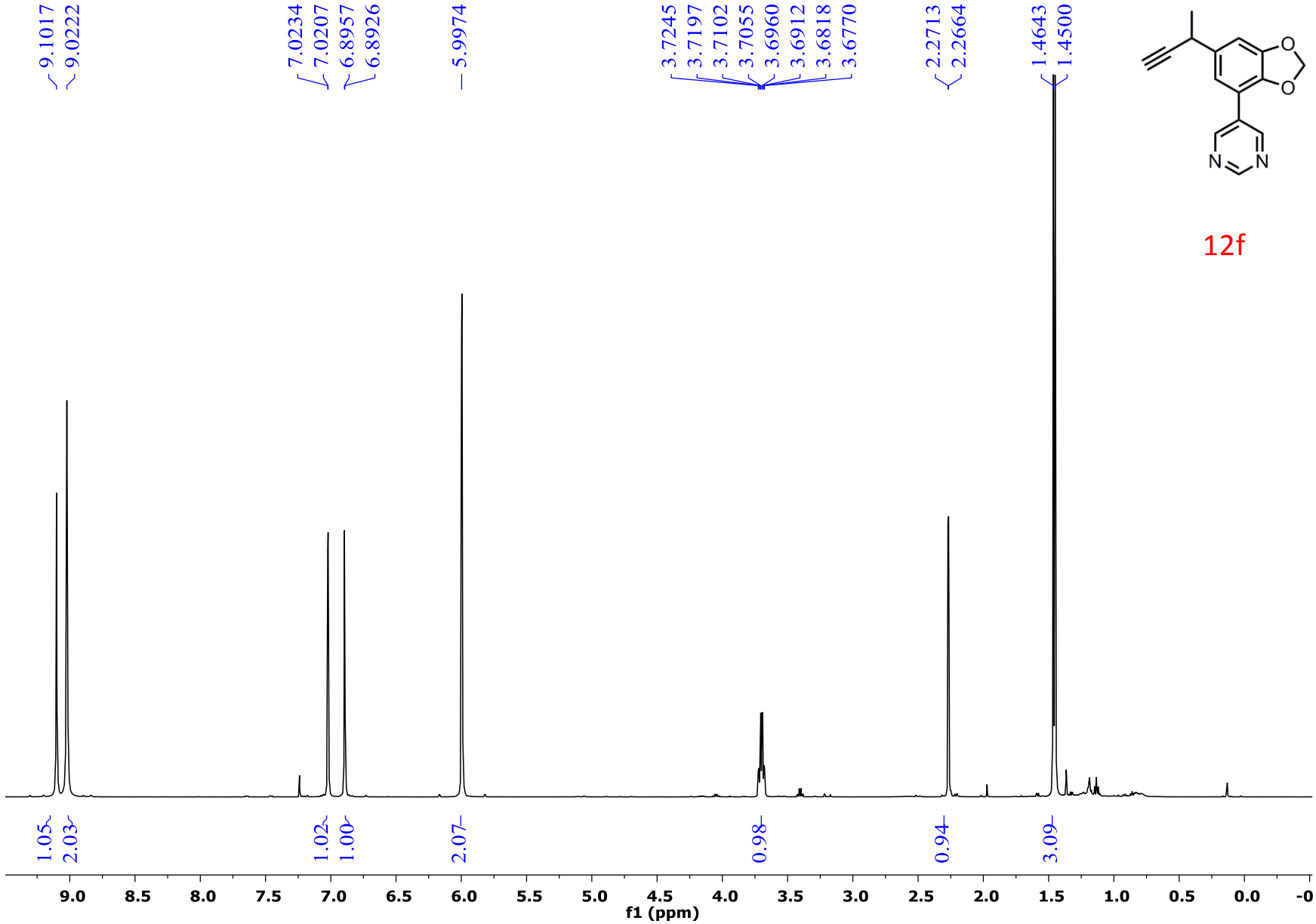
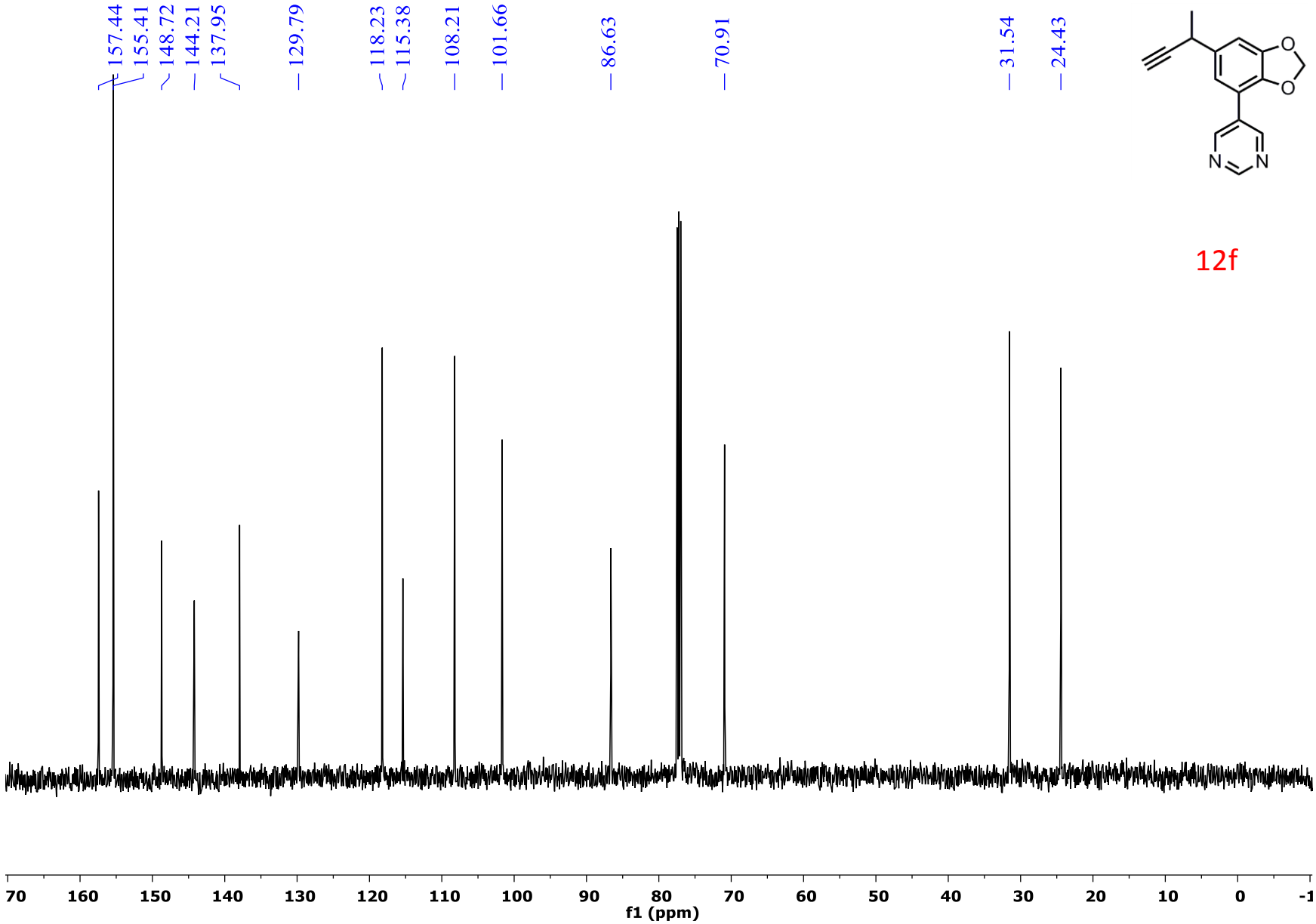
152.66
144.06
142.13
141.77
131.75
128.94
126.83
126.49
110.88
87.13
70.13
55.65
25.64
22.65
O
N
N
12e
70
160
150
140
130
120
110
100
90
80
f1 (ppm)
70
60
50
40
30
20
10
0
-1


9.1017
9.0222
7.0234
7.0207
6.8957
6.8926
5.9974
3.7245
3.7197
3.7102
3.7055
3.6960
3.6912
3.6818
3.6770
2.2713
2.2664
1.4643
1.4500
12f
1.05
2.03
1.02
1.00
2.07
0.98
0.94
3.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)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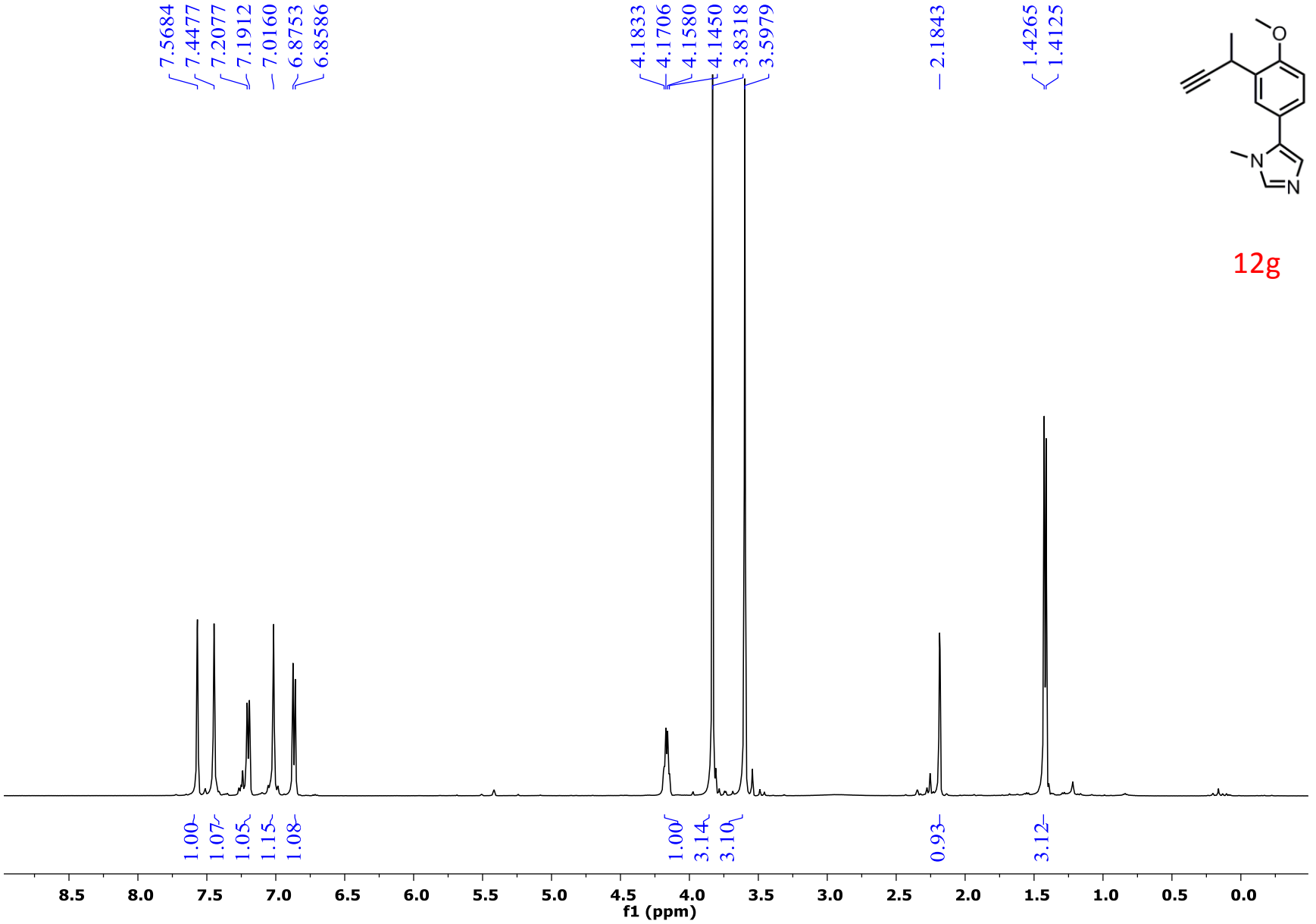
155.41
148.72
144.21
137.95
129.79
118.23
115.38
108.21
101.66
86.63
70.91
31.54
24.43
O
O
N
N
12f
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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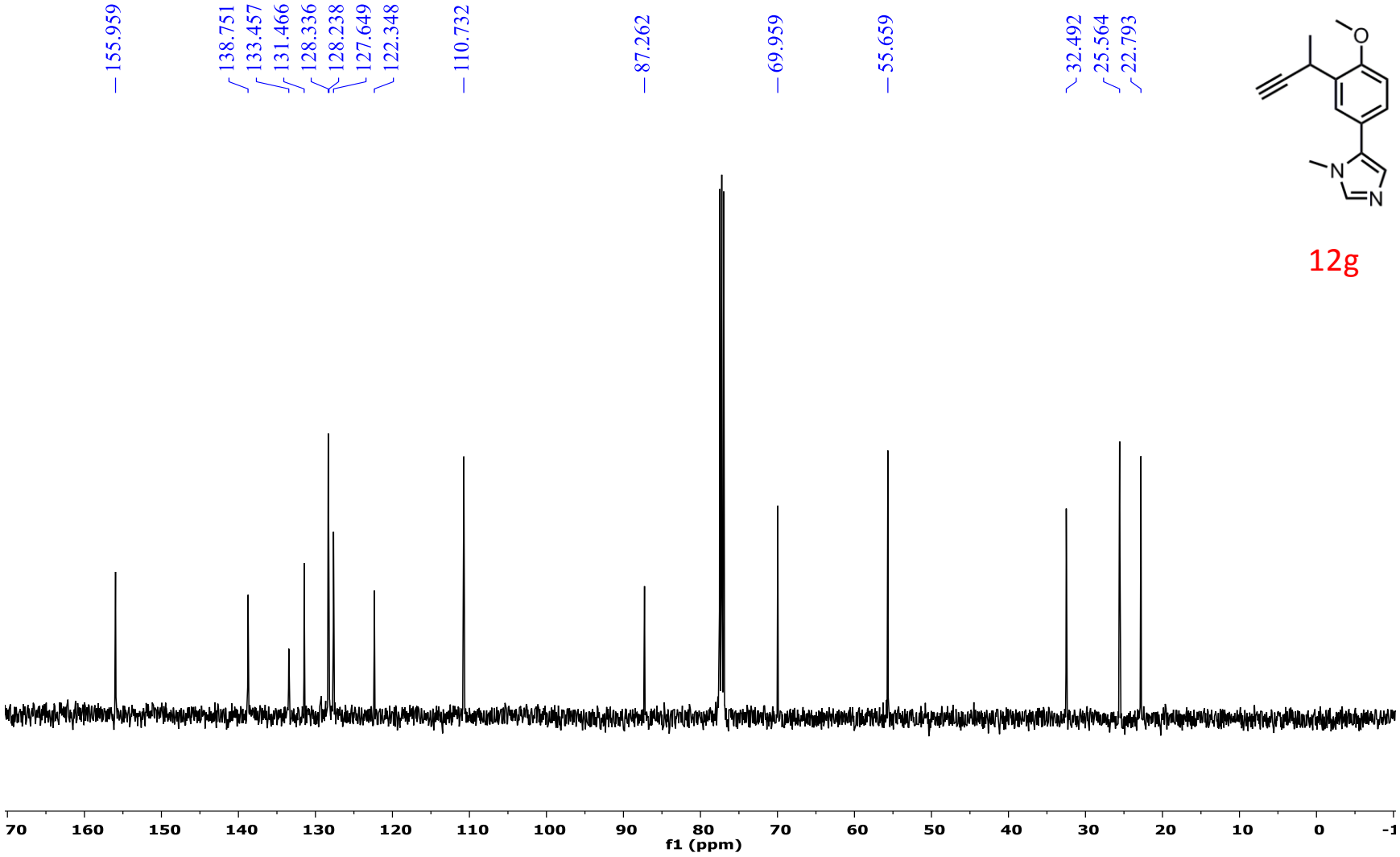
7.4477
7.2077
7.1912
7.0160
6.8753
6.8586
4.1833
4.1706
4.1580
4.1450
3.8318
3.5979
2.1843
1.4265
1.4125
O
N
N
12g
1.00
1.07
1.05
1.15
1.08
1.00
3.14
3.10
0.93
3.12
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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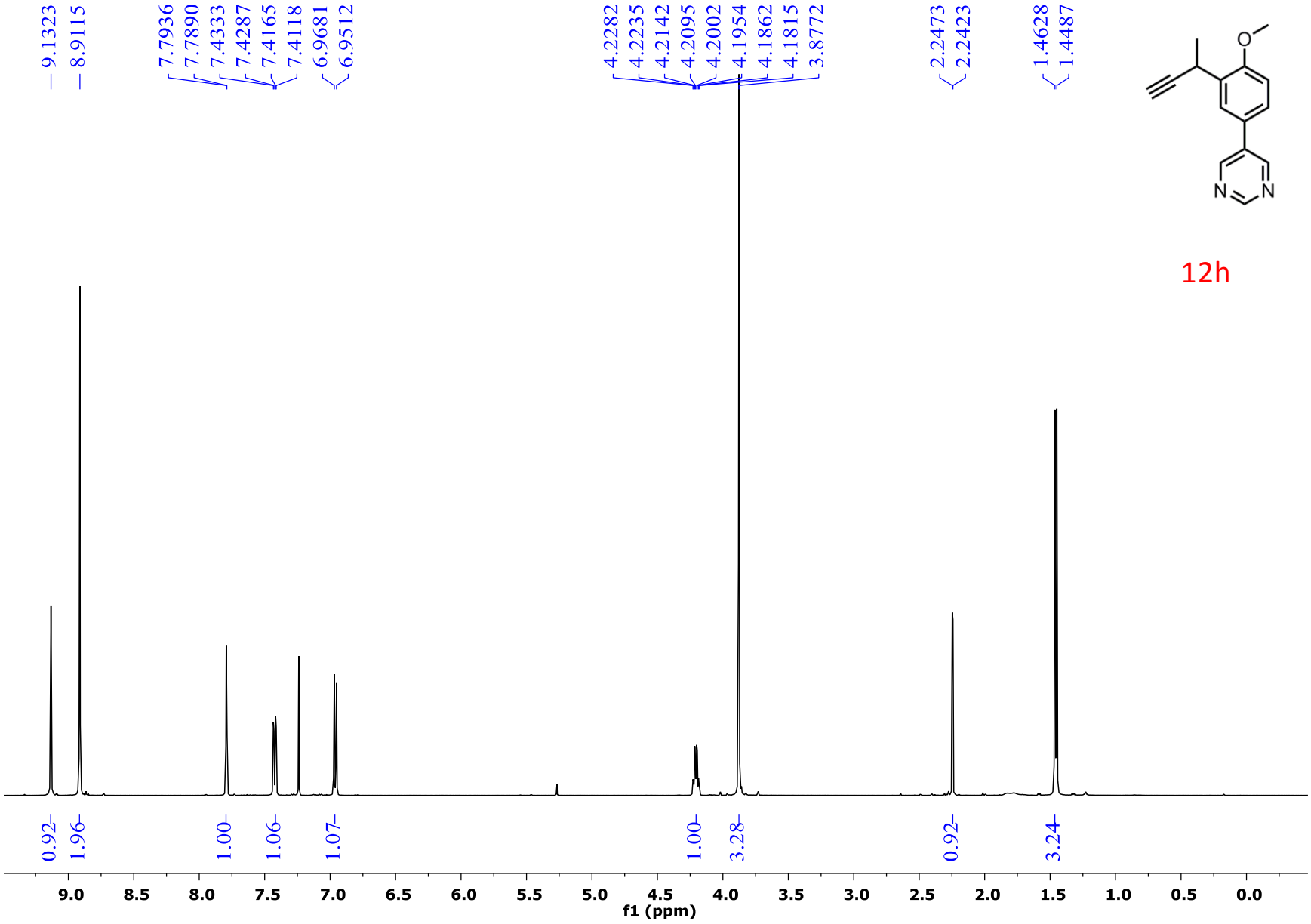
138.751
133.457
131.466
128.336
128.238
127.649
122.348
110.732
87.262
69.959
55.659
32.492
25.564
22.793
O
N
N
12g
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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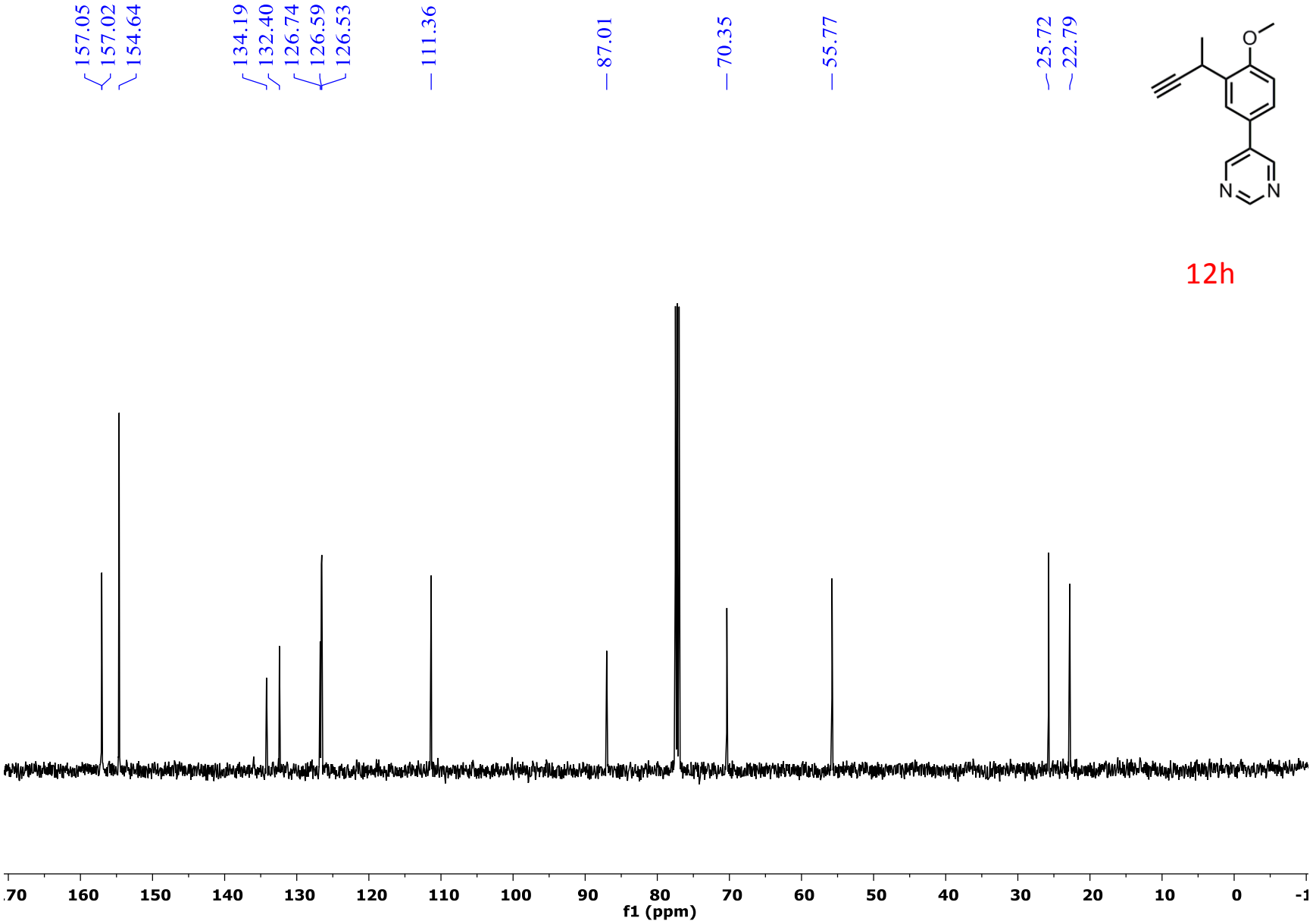
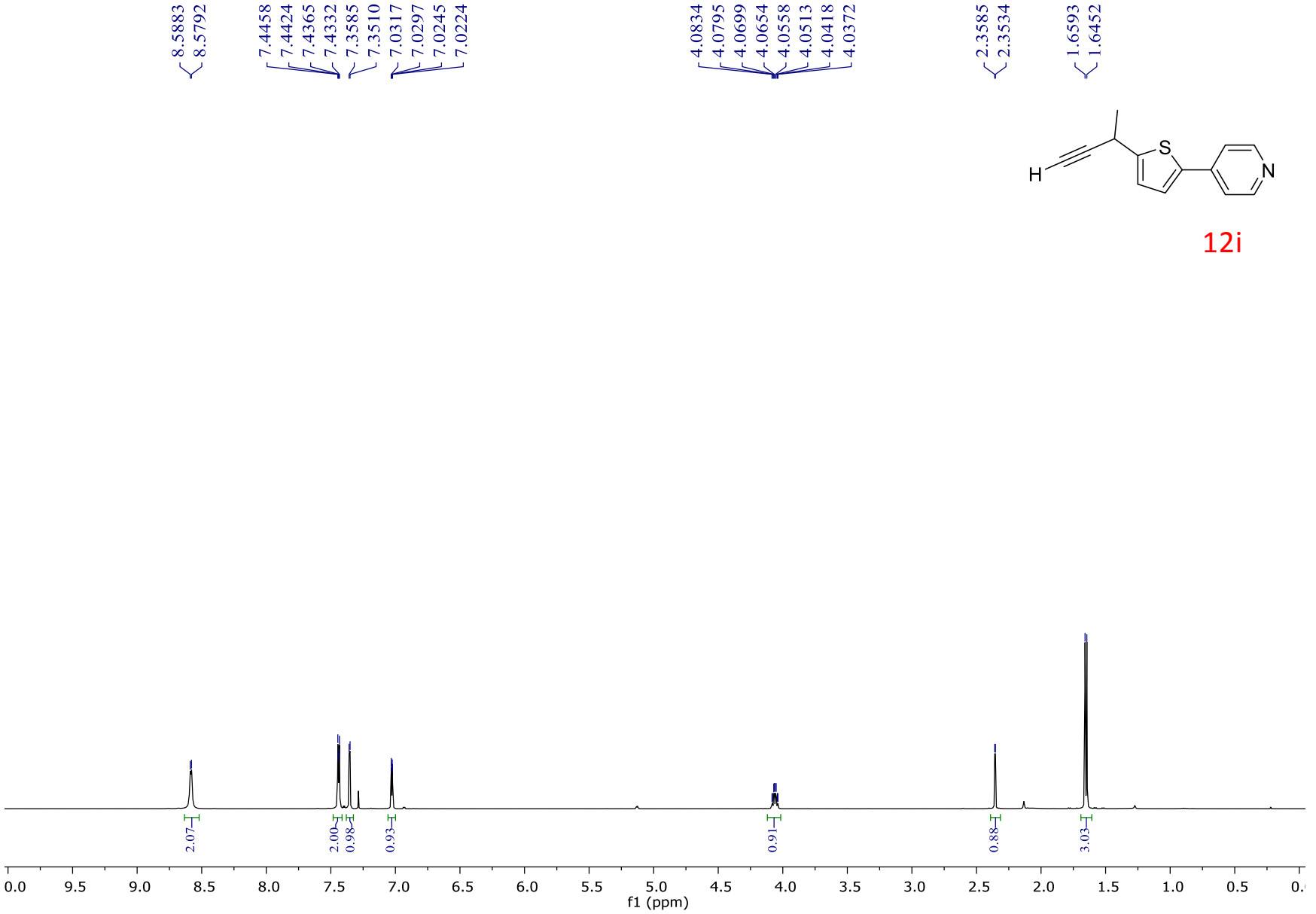
8.9115
7.7936
7.7890
7.4333
7.4287
7.4165
7.4118
6.9681
6.9512
4.2282
4.2235
4.2142
4.2095
4.2002
4.1954
4.1862
4.1815
3.8772
2.2473
2.2423
1.4628
1.4487
O
N
N
12h
0.92
1.96
1.00
1.06
1.07
1.00
3.28
0.92
3.24
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.05
157.02
154.64
134.19
132.40
126.74
126.59
126.53
111.36
87.01
70.35
55.77
25.72
22.79
O
N
N
12h
f1 (ppm)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8.5792
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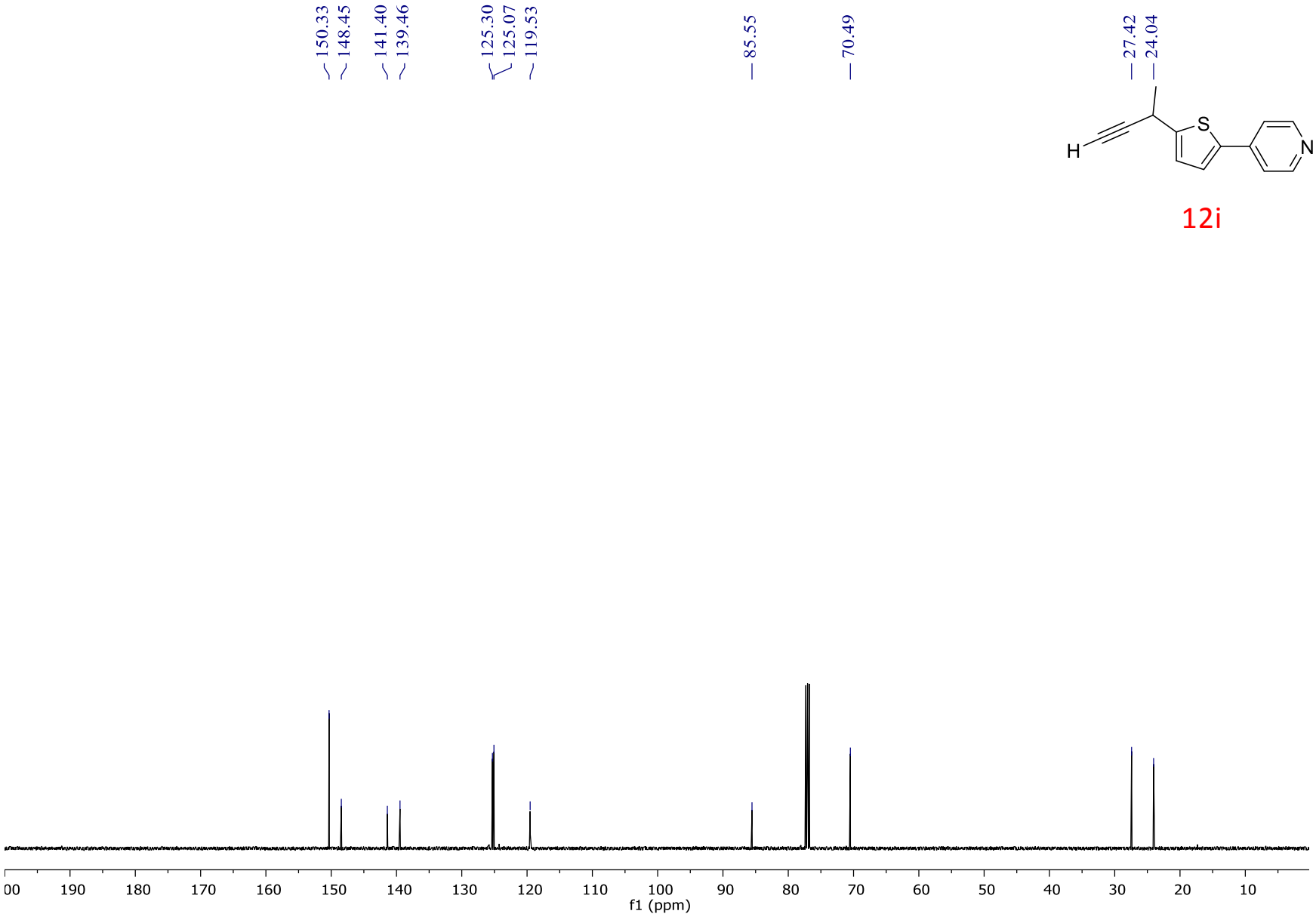
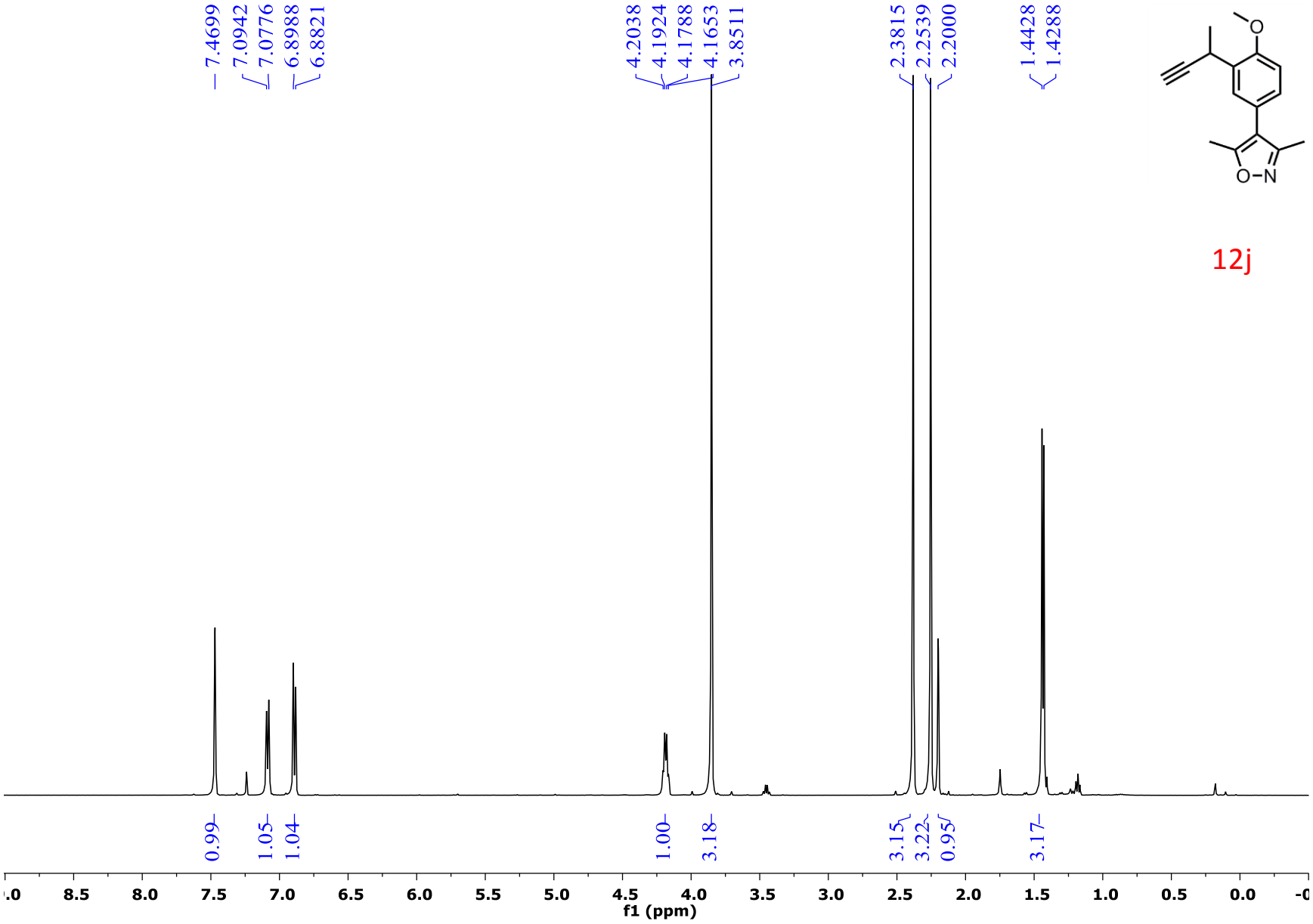
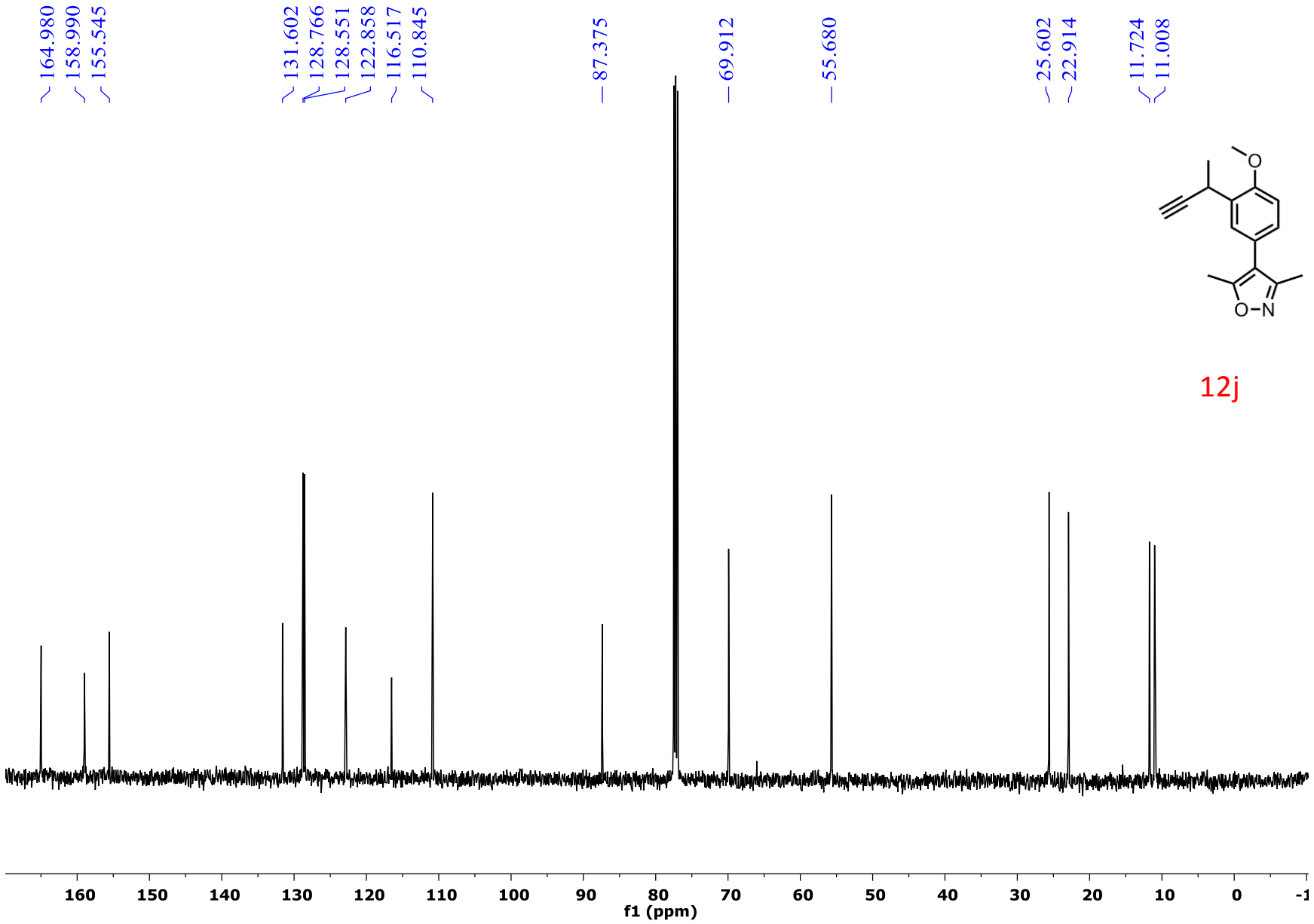
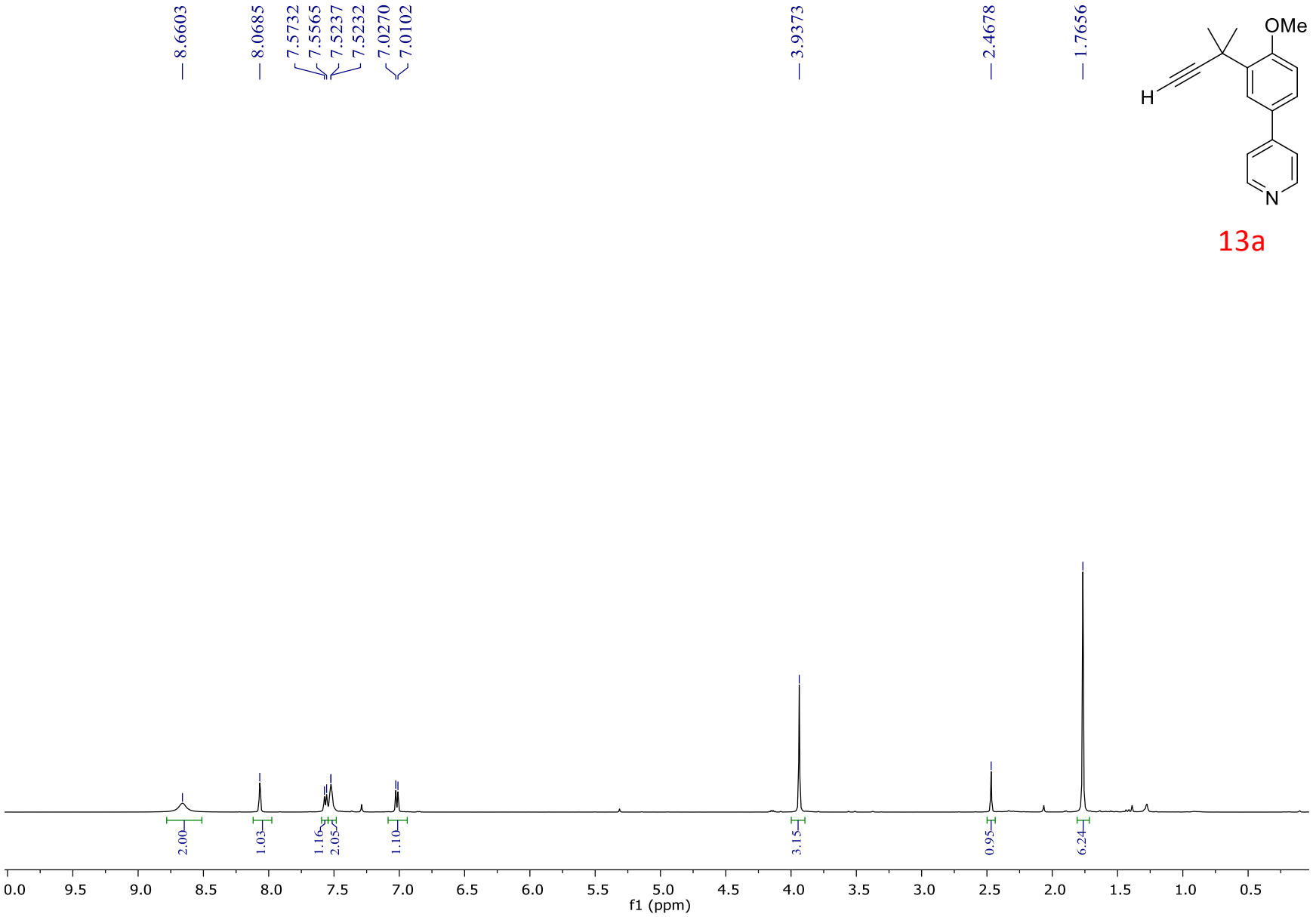
7.4424
7.4365
7.4332
7.3585
7.3510
7.0317
7.0297
7.0245
7.0224
4.0834
4.0795
4.0699
4.0654
4.0558
4.0513
4.0418
4.0372
2.3585
2.3534
1.6593
1.6452
H
S
N
12i
2.07
2.00
0.98
0.93
0.91
0.88
3.03
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


150.33
148.45
141.40
139.46
125.30
125.07
119.53
85.55
70.49
27.42
24.04
S
N
H
f1 (ppm)

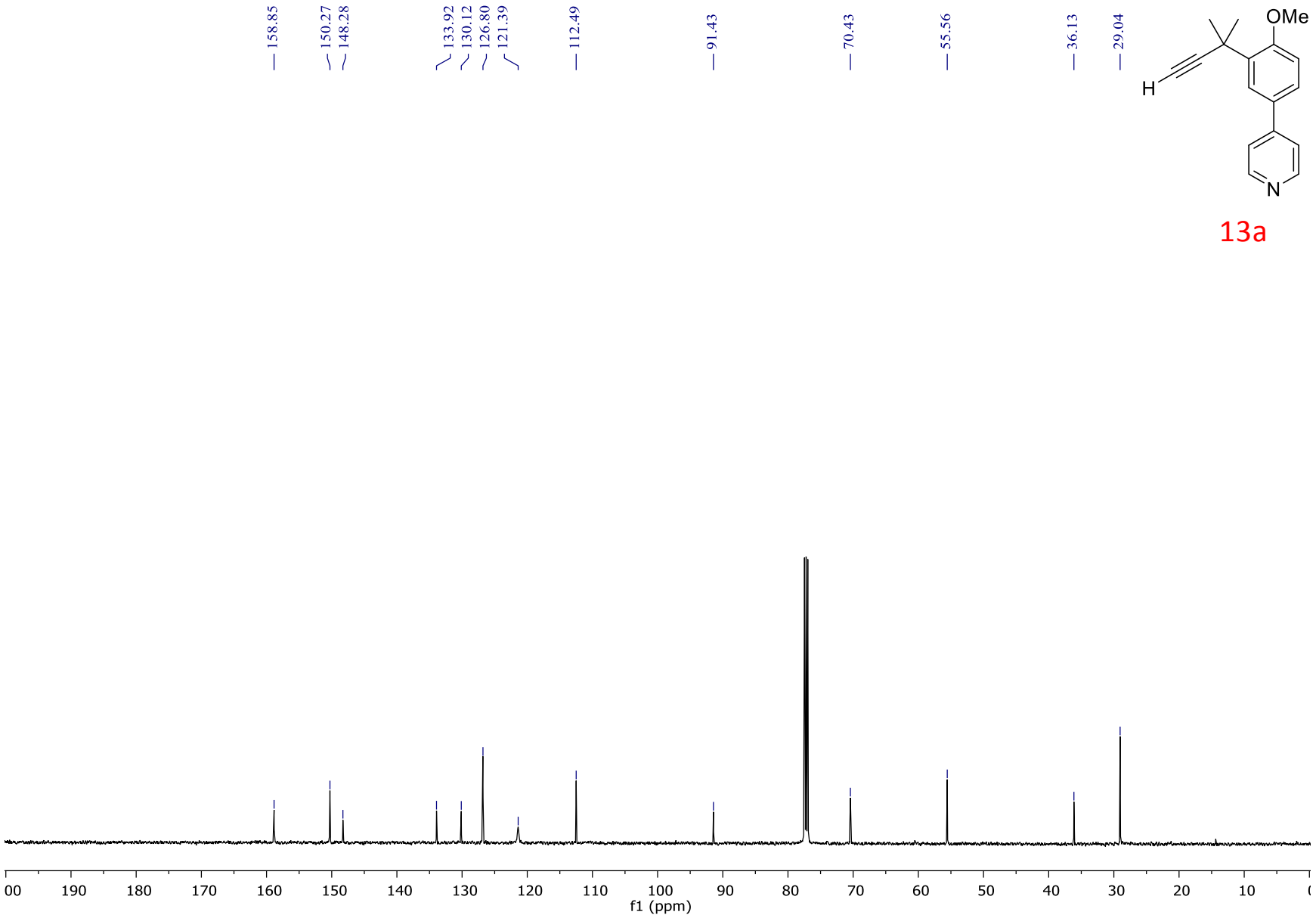
12i

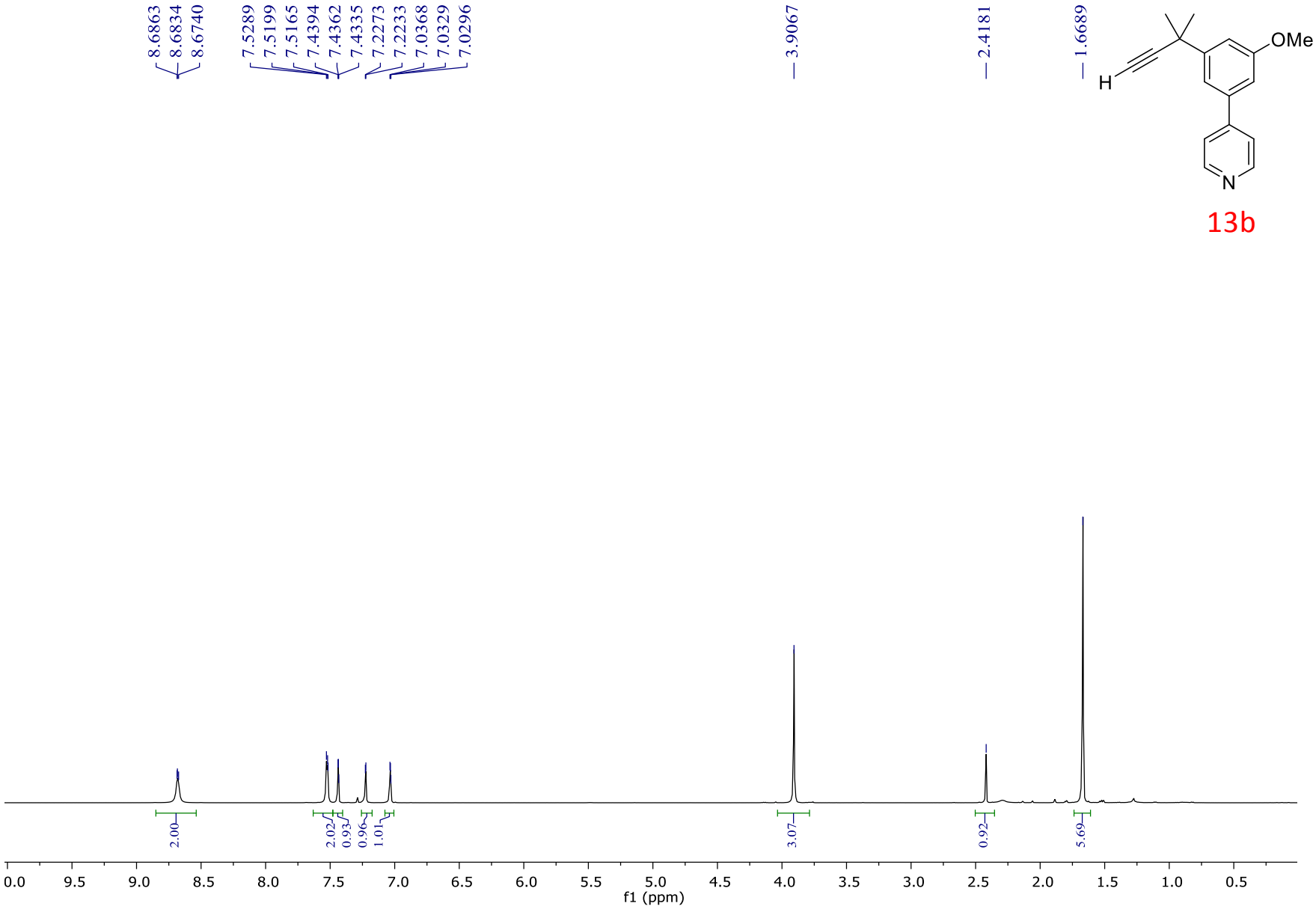

7.4699
7.0942
7.0776
6.8988
6.8821
4.2038
4.1924
4.1788
4.1653
3.8511
2.3815
2.2539
2.2000
1.4428
1.4288
O
O-N
12j
0.99
1.05
1.04
1.00
3.18
3.15
3.22
0.95
3.17
f1 (ppm)

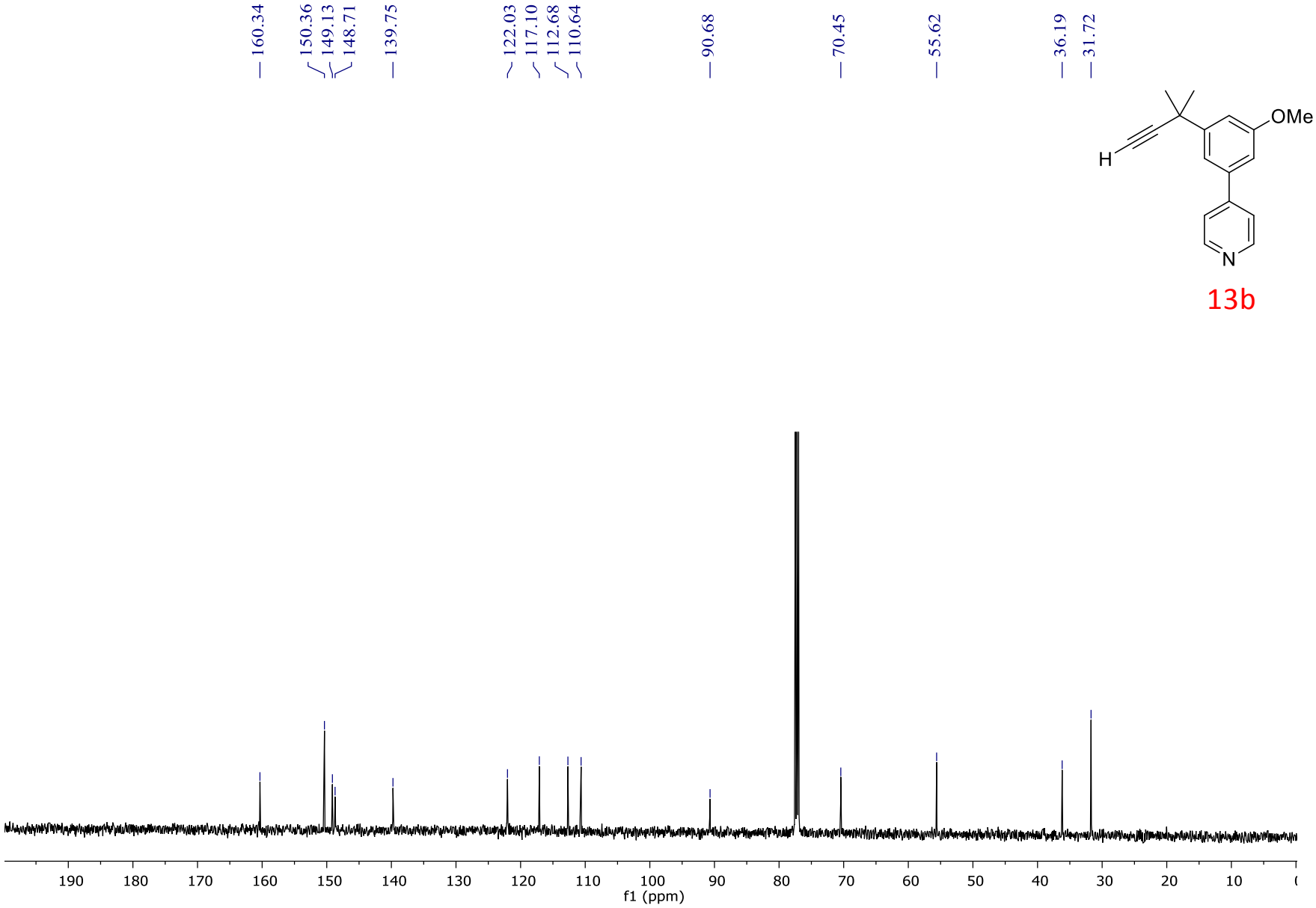

164.980
158.990
155.545
131.602
128.766
128.551
122.858
116.517
110.845
87.375
69.912
55.680
25.602
22.914
11.724
11.008
O
O-N
12j
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

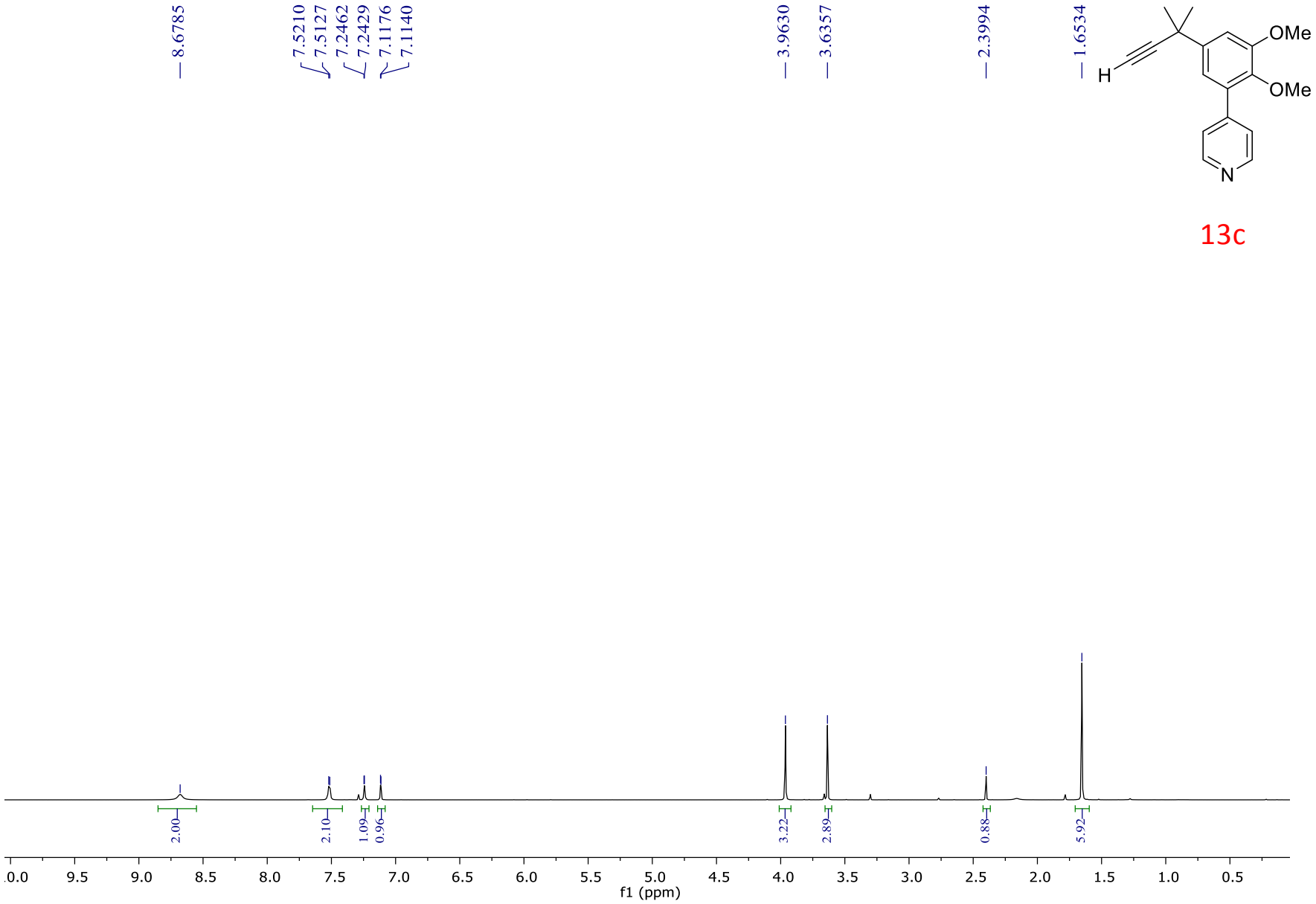

8.6603
8.0685
7.5732
7.5565
7.5237
7.5232
7.0270
7.0102
3.9373
2.4678
1.7656
OMe
H
N
2.00
1.03
1.16
2.05
1.10
3.15
0.95
6.24
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

13a

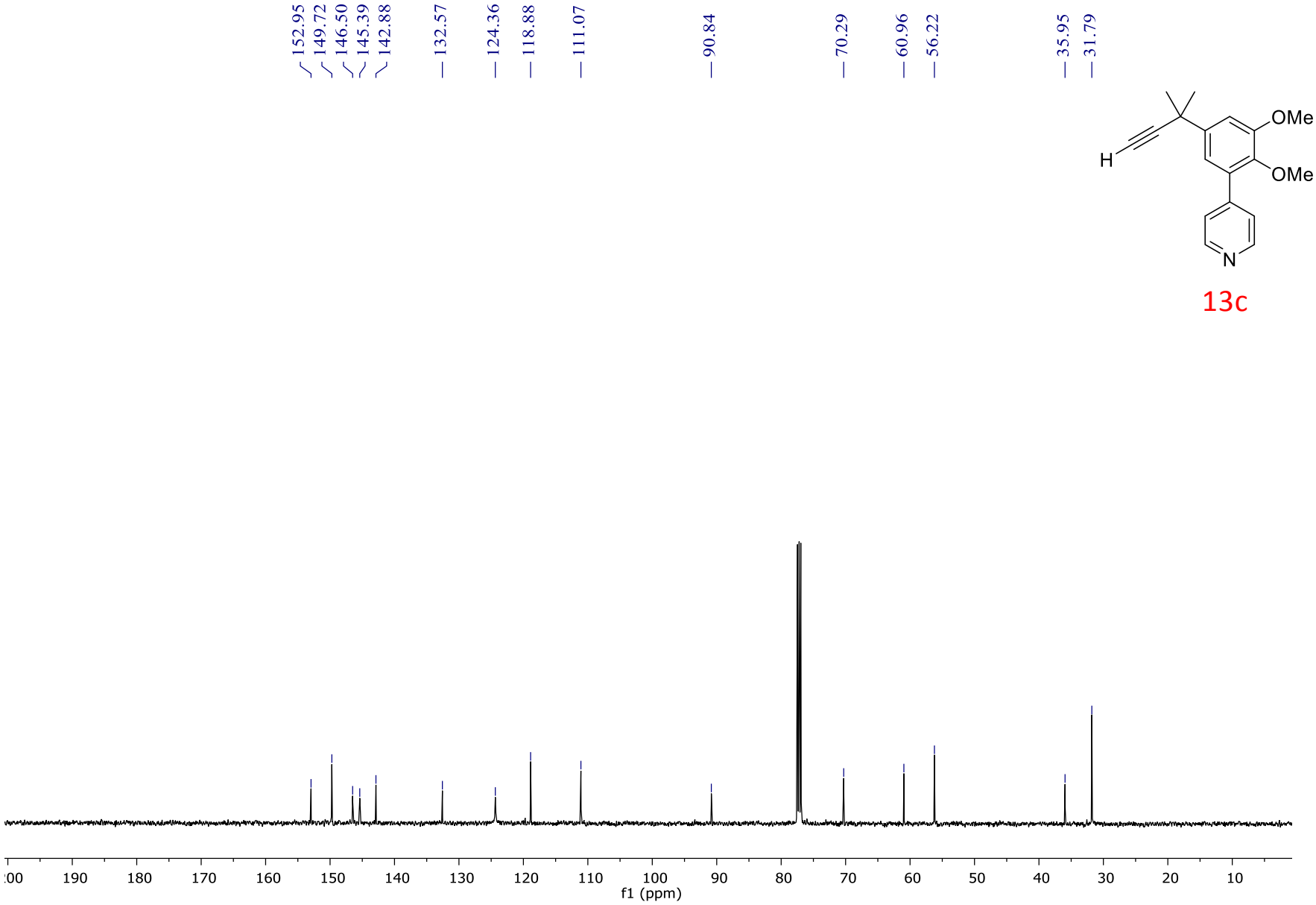

158.85
150.27
148.28
133.92
130.12
126.80
121.39
112.49
91.43
70.43
55.56
36.13
29.04
OMe
H
N
13a
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

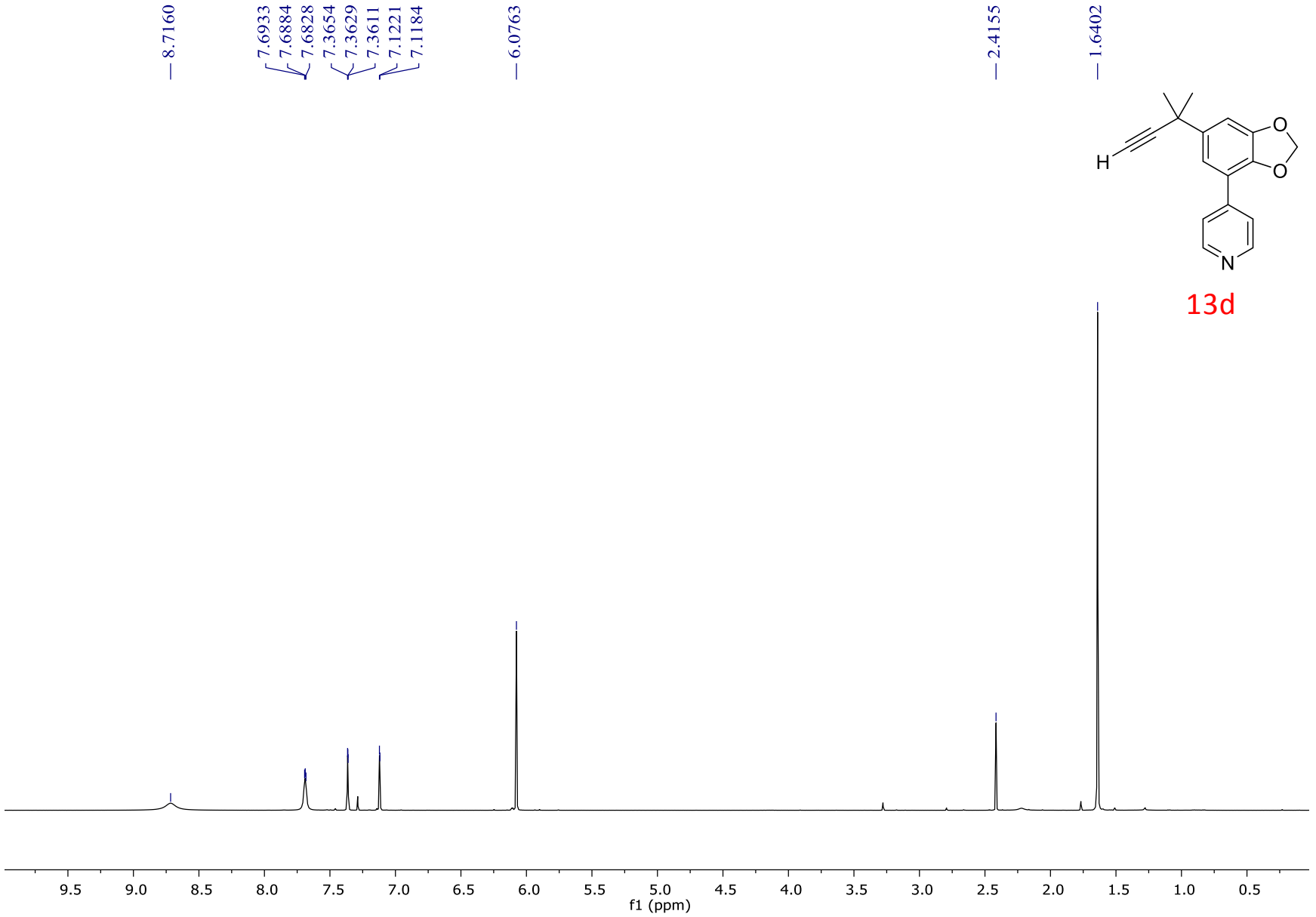

8.6863
8.6834
8.6740
7.5289
7.5199
7.5165
7.4394
7.4362
7.4335
7.2273
7.2233
7.0368
7.0329
7.0296
3.9067
2.4181
1.6689
OMe
H
N
13b
2.00
2.02
0.93
0.96
1.01
3.07
0.92
5.69
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

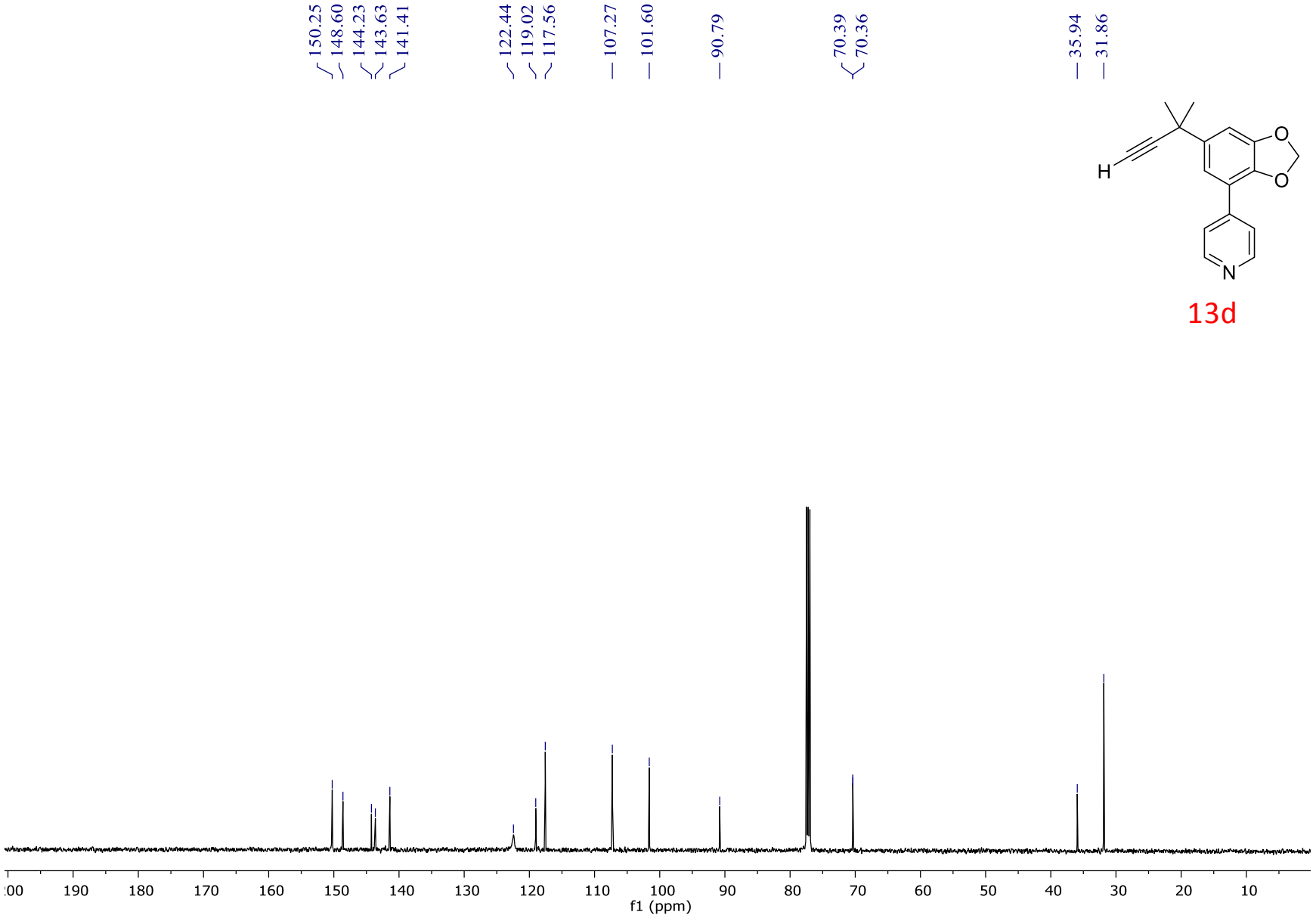

160.34
150.36
149.13
148.71
139.75
122.03
117.10
112.68
110.64
90.68
70.45
55.62
36.19
31.72
OMe
H
N
13b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.6785
7.5210
7.5127
7.2462
7.2429
7.1176
7.1140
3.9630
3.6357
2.3994
1.6534
OMe
OMe
H
N
2.00
2.10
1.09
0.96
3.22
2.89
0.88
5.92
f1 (ppm)

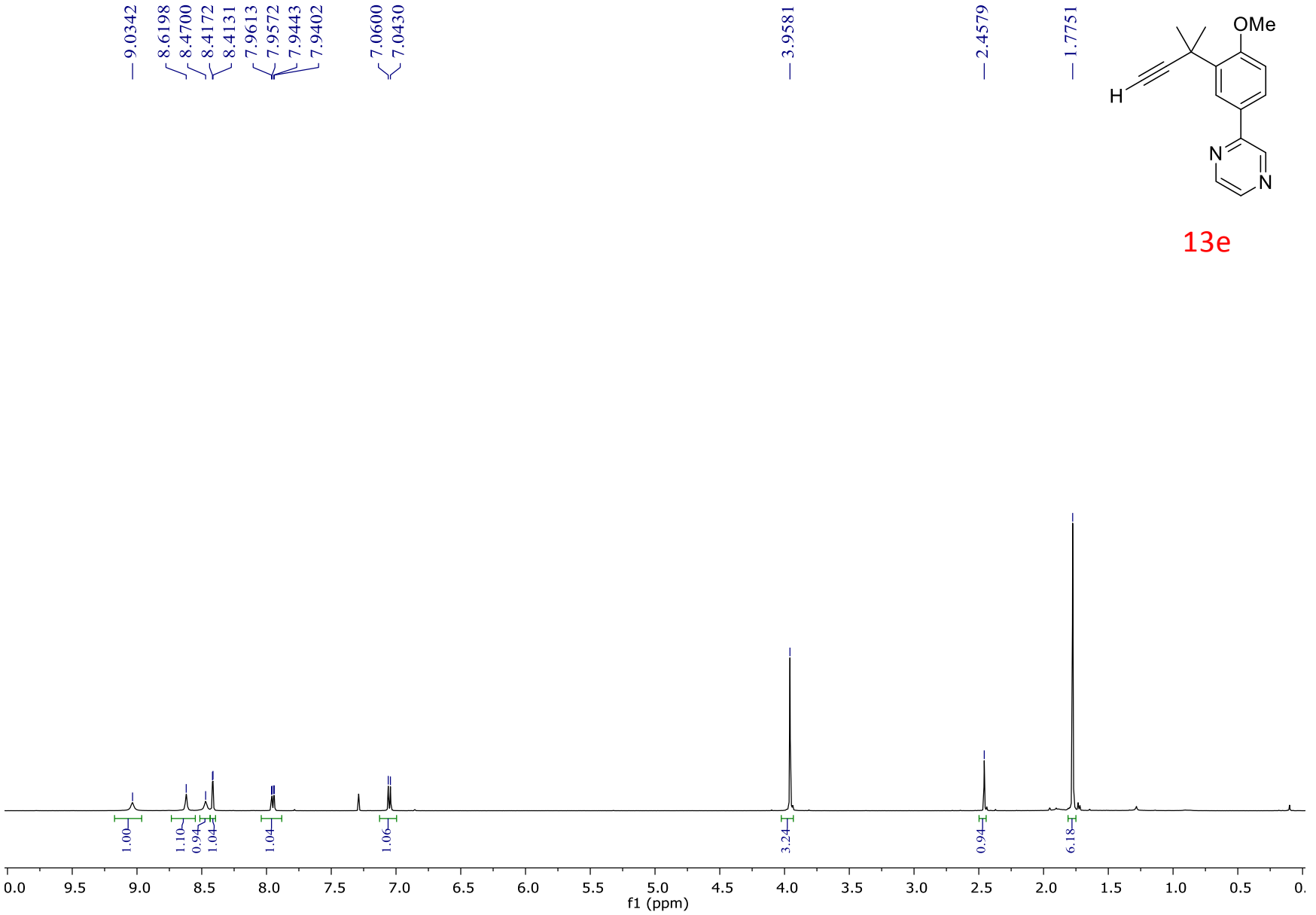
13c


152.95
149.72
146.50
145.39
142.88
132.57
124.36
118.88
111.07
90.84
70.29
60.96
56.22
35.95
31.79
OMe
OMe
H
N
13c
f1 (ppm)

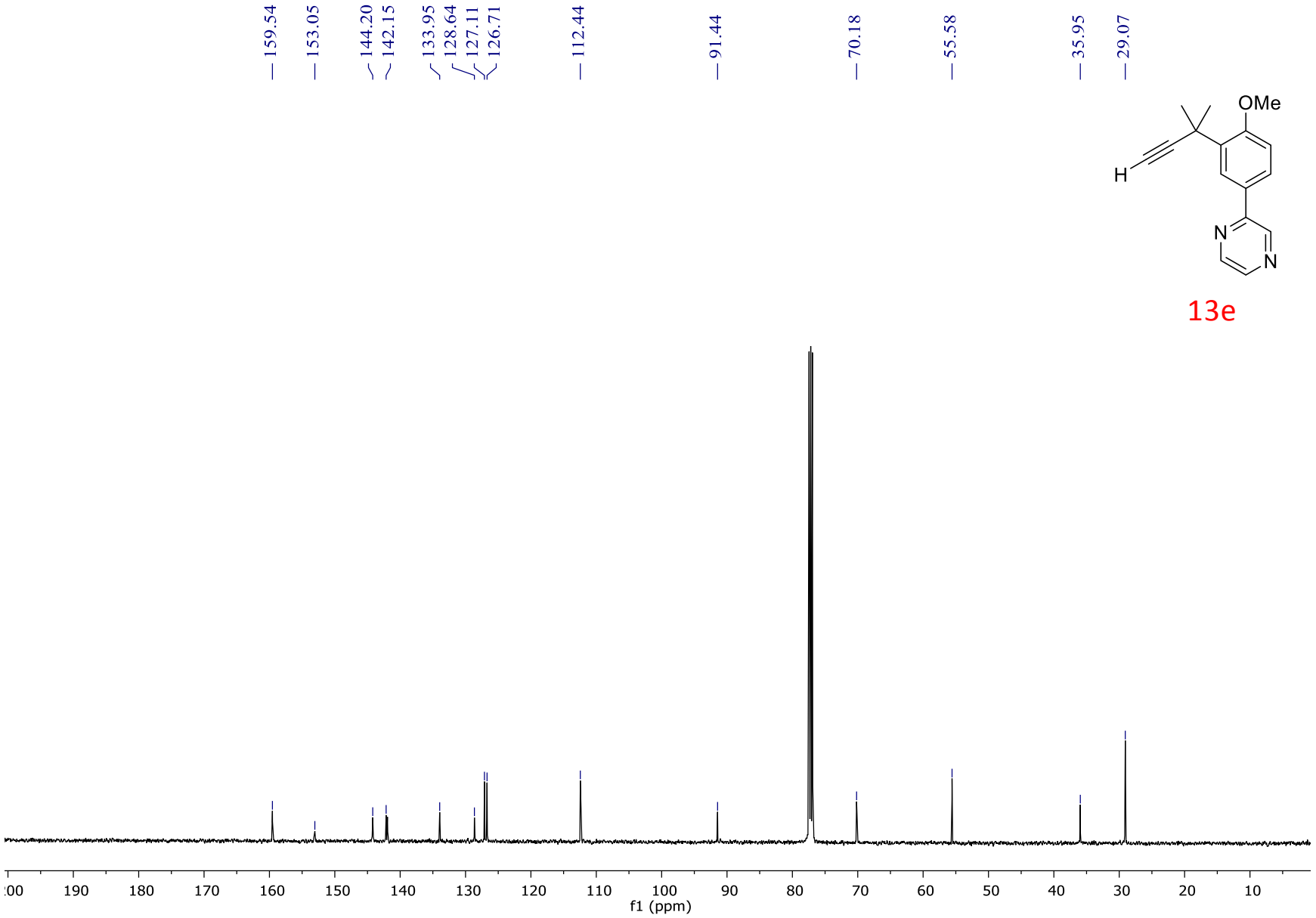

8.7160
7.6933
7.6884
7.6828
7.3654
7.3629
7.3611
7.1221
7.1184
6.0763
2.4155
1.6402
H
O
O
N
13d
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

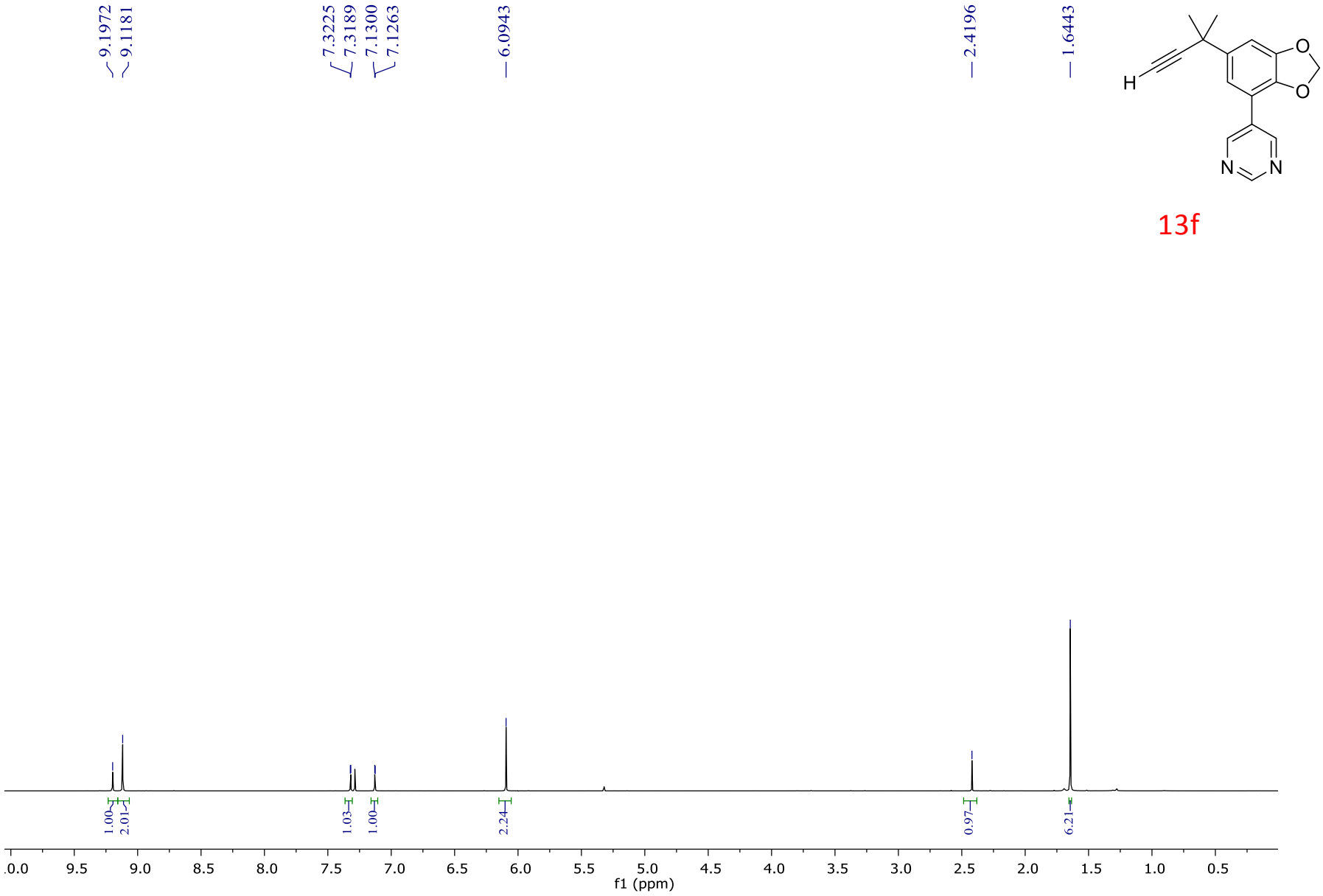

150.25
148.60
144.23
143.63
141.41
122.44
119.02
117.56
107.27
101.60
90.79
70.39
70.36
35.94
31.86
H
O
O
N
f1 (ppm)

13d


9.0342
8.6198
8.4700
8.4172
8.4131
7.9613
7.9572
7.9443
7.9402
7.0600
7.0430
3.9581
2.4579
1.7751
OMe
H
N
N
1.00
1.10
0.94
1.04
1.04
1.06
3.24
0.94
6.18
f1 (ppm)

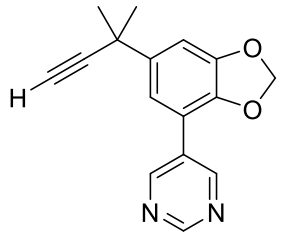
13e


159.54
153.05
144.20
142.15
133.95
128.64
127.11
126.71
112.44
91.44
70.18
55.58
35.95
29.07
OMe
H
N
N
13e
f1 (ppm)

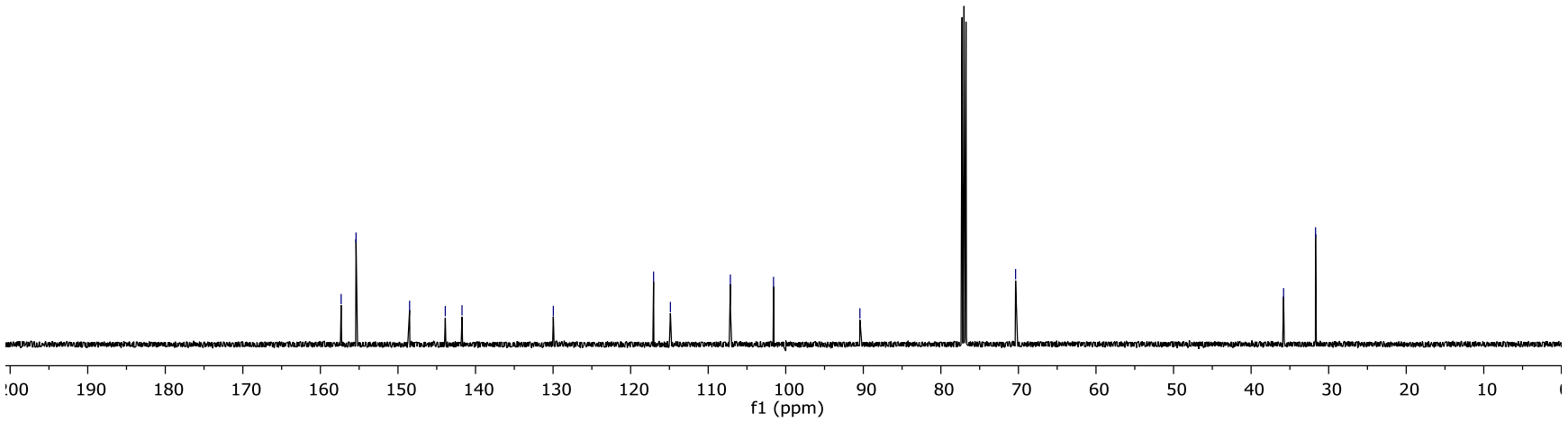

9.1972
9.1181
7.3225
7.3189
7.1300
7.1263
6.0943
2.4196
1.6443
H
O
O
N
N
1.00
2.01
1.03
1.00
2.24
0.97
6.21
f1 (ppm)

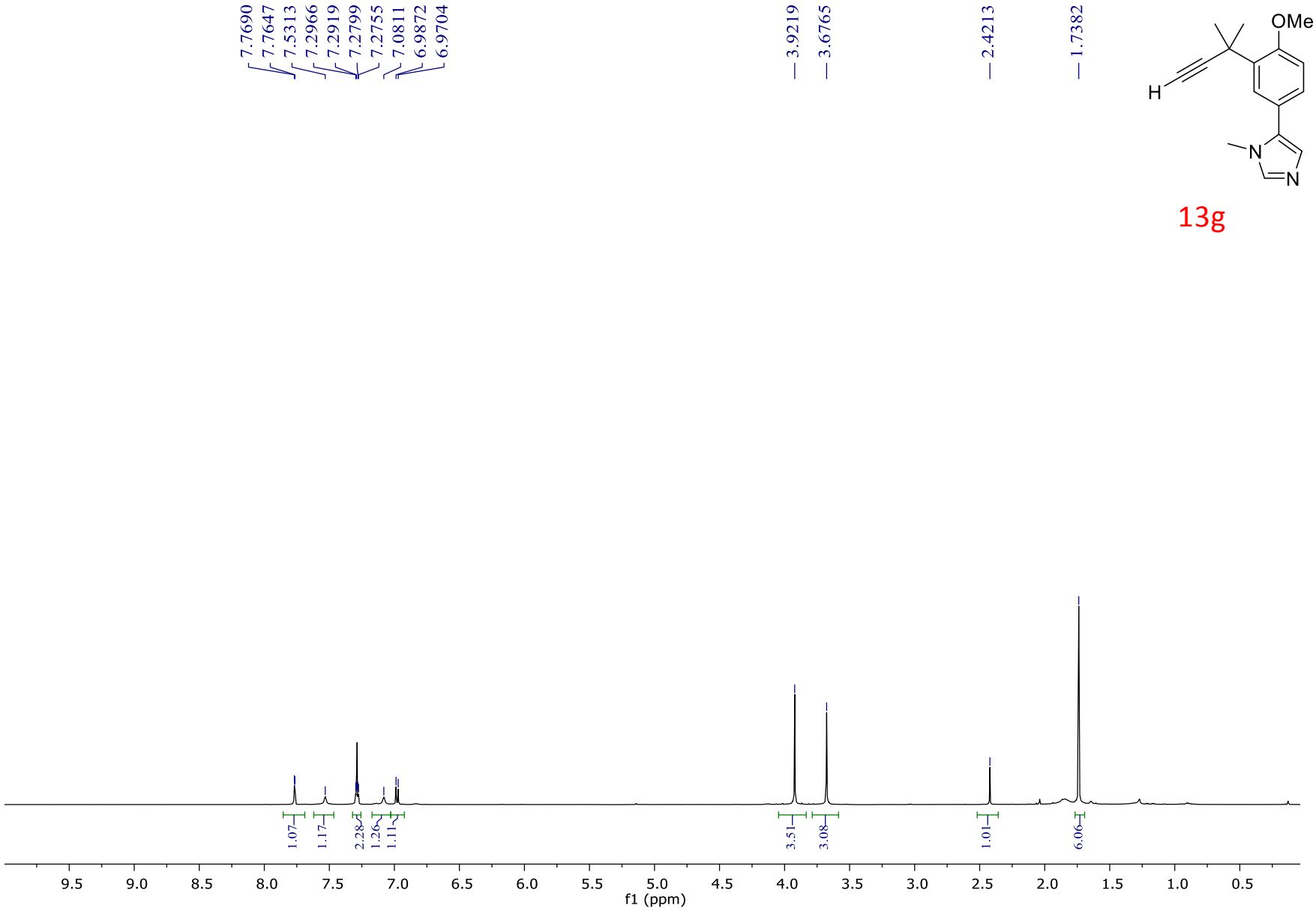
13f

157.33
155.40
148.50
143.90
141.74
129.97
117.04
114.87
107.14
101.58
90.44
70.37
35.81
31.69

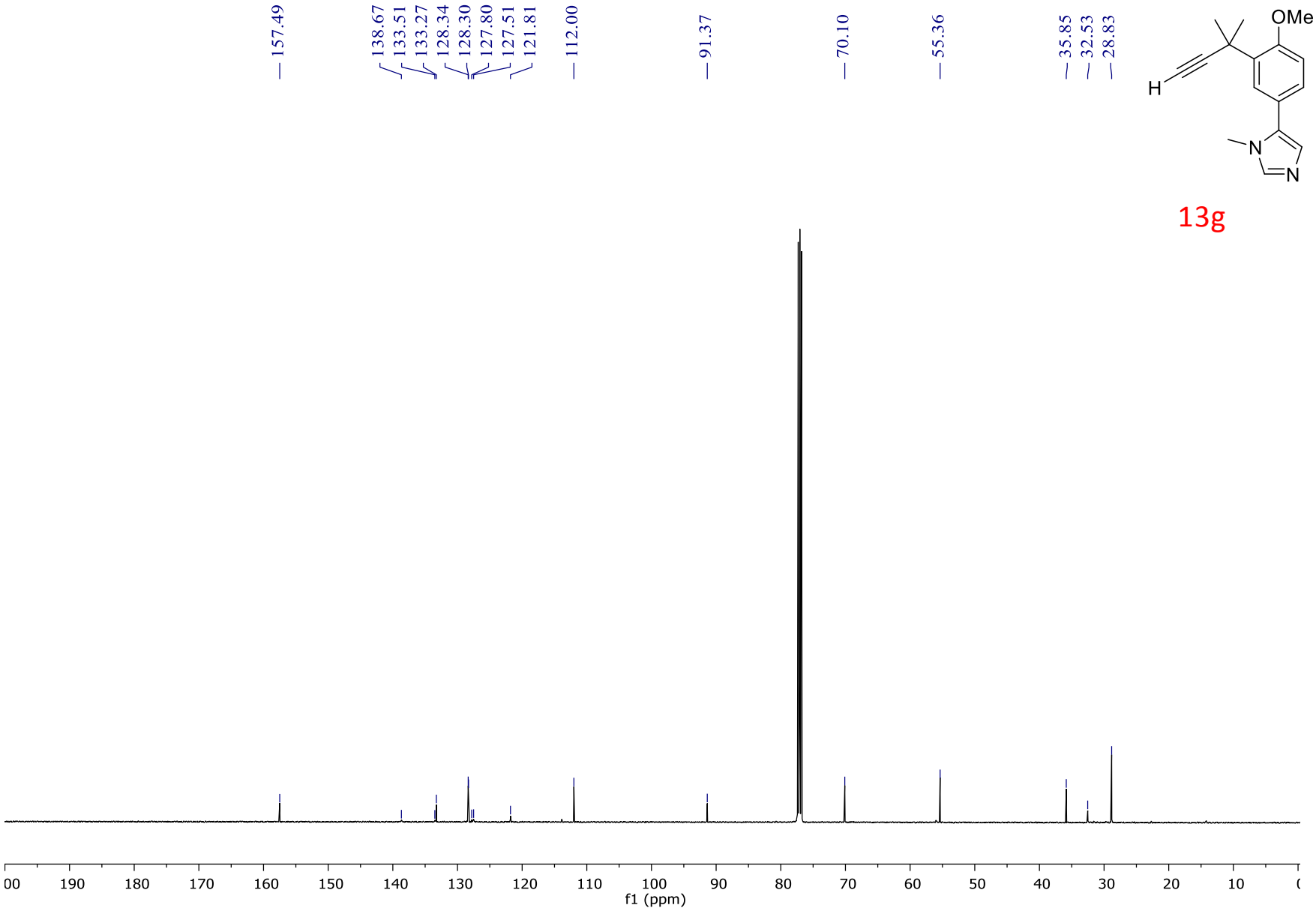


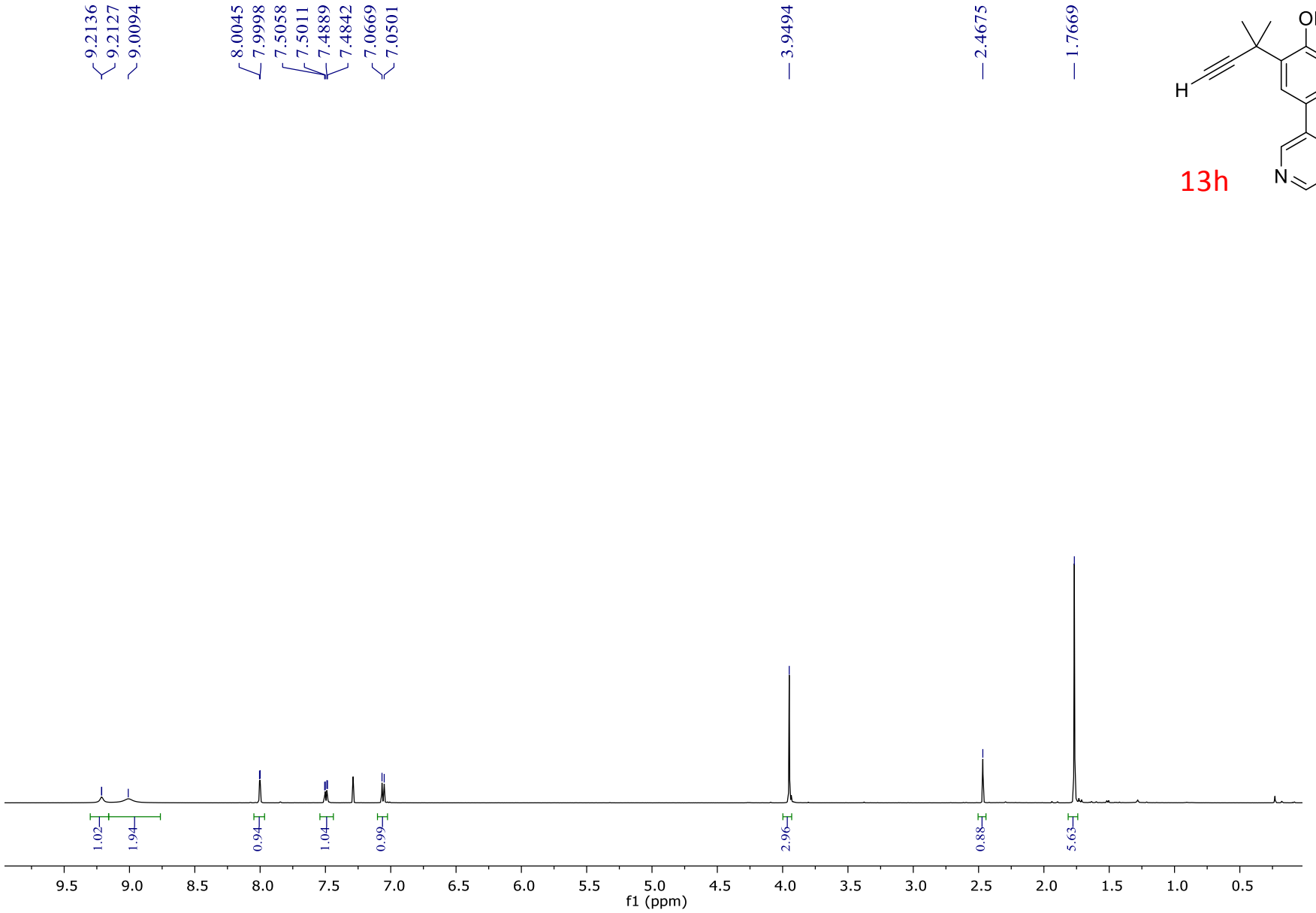
13f



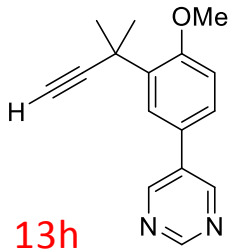

7.7690
7.7647
7.5313
7.2966
7.2919
7.2799
7.2755
7.0811
6.9872
6.9704
3.9219
3.6765
2.4213
1.7382
OMe
H
N
N
1.07
1.17
2.28
1.26
1.11
3.51
3.08
1.01
6.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

13g

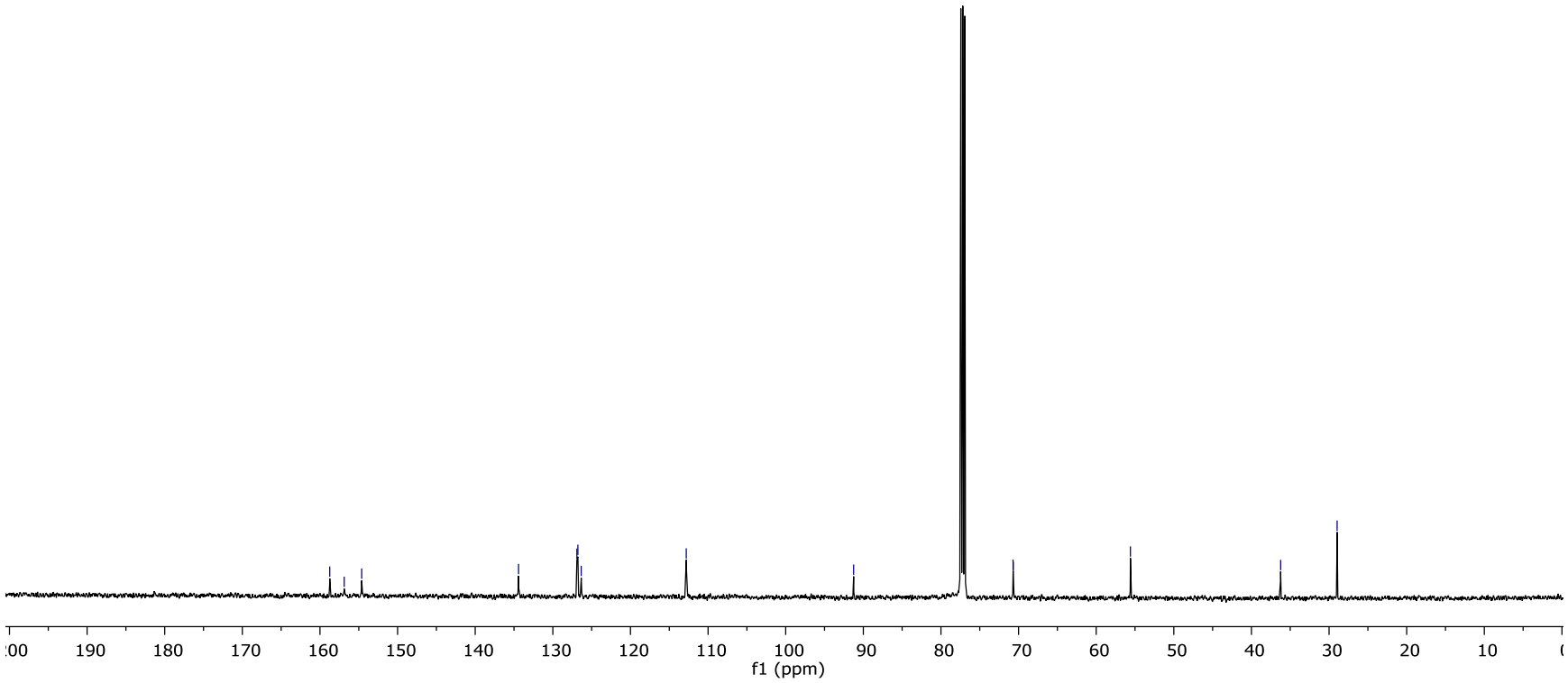

157.49
138.67
133.51
133.27
128.34
128.30
127.80
127.51
121.81
112.00
91.37
70.10
55.36
35.85
32.53
28.83
OMe
H
N
N
13g
f1 (ppm)

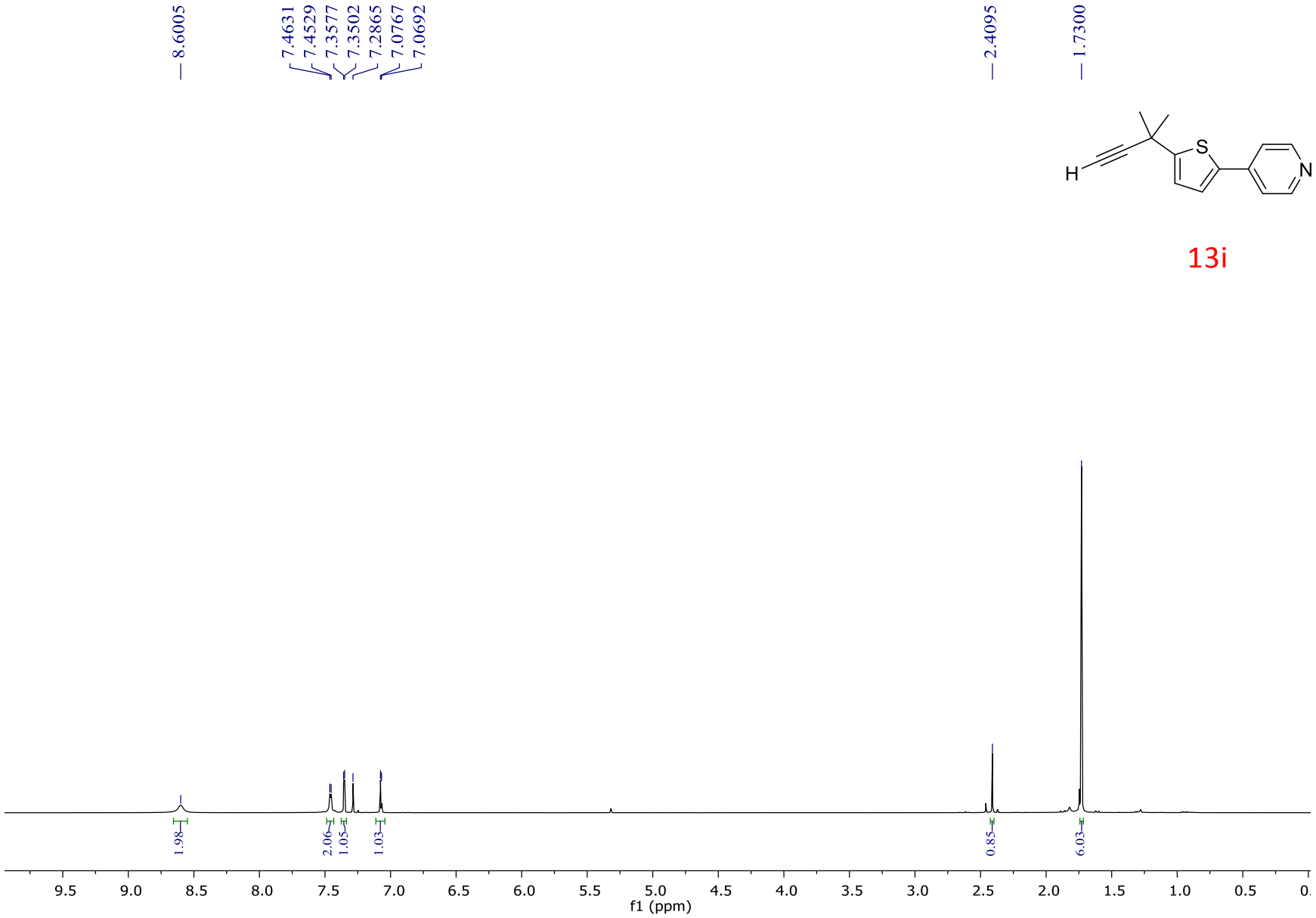

9.2136
9.2127
9.0094
8.0045
7.9998
7.5058
7.5011
7.4889
7.4842
7.0669
7.0501
3.9494
2.4675
1.7669
OMe
H
N
N
13h
1.02
1.94
0.94
1.04
0.99
2.96
0.88
5.63
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

158.74
156.88
154.63
134.41
126.90
126.77
126.34
112.81
91.25
70.71
70.69
55.59
36.24
28.96

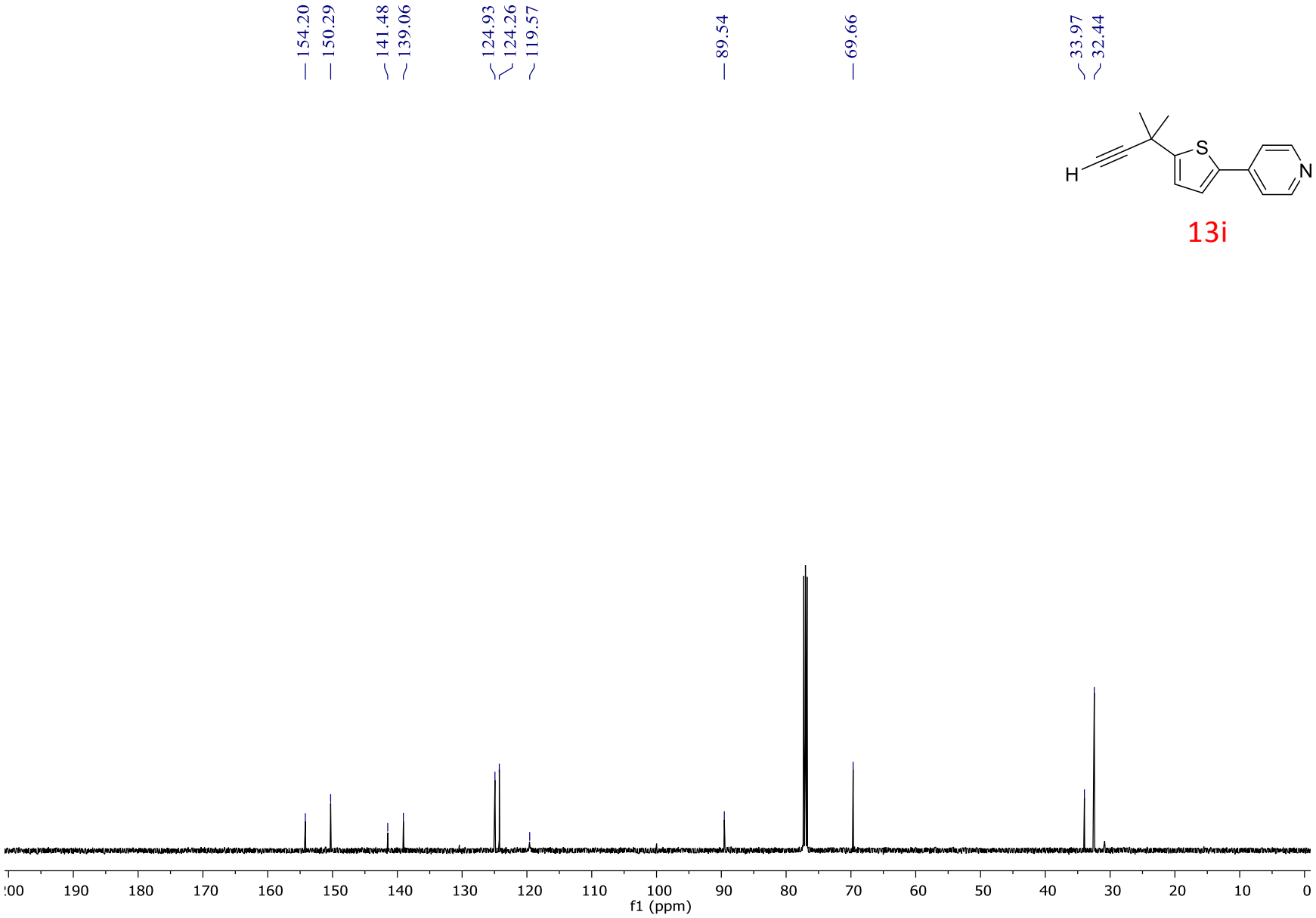


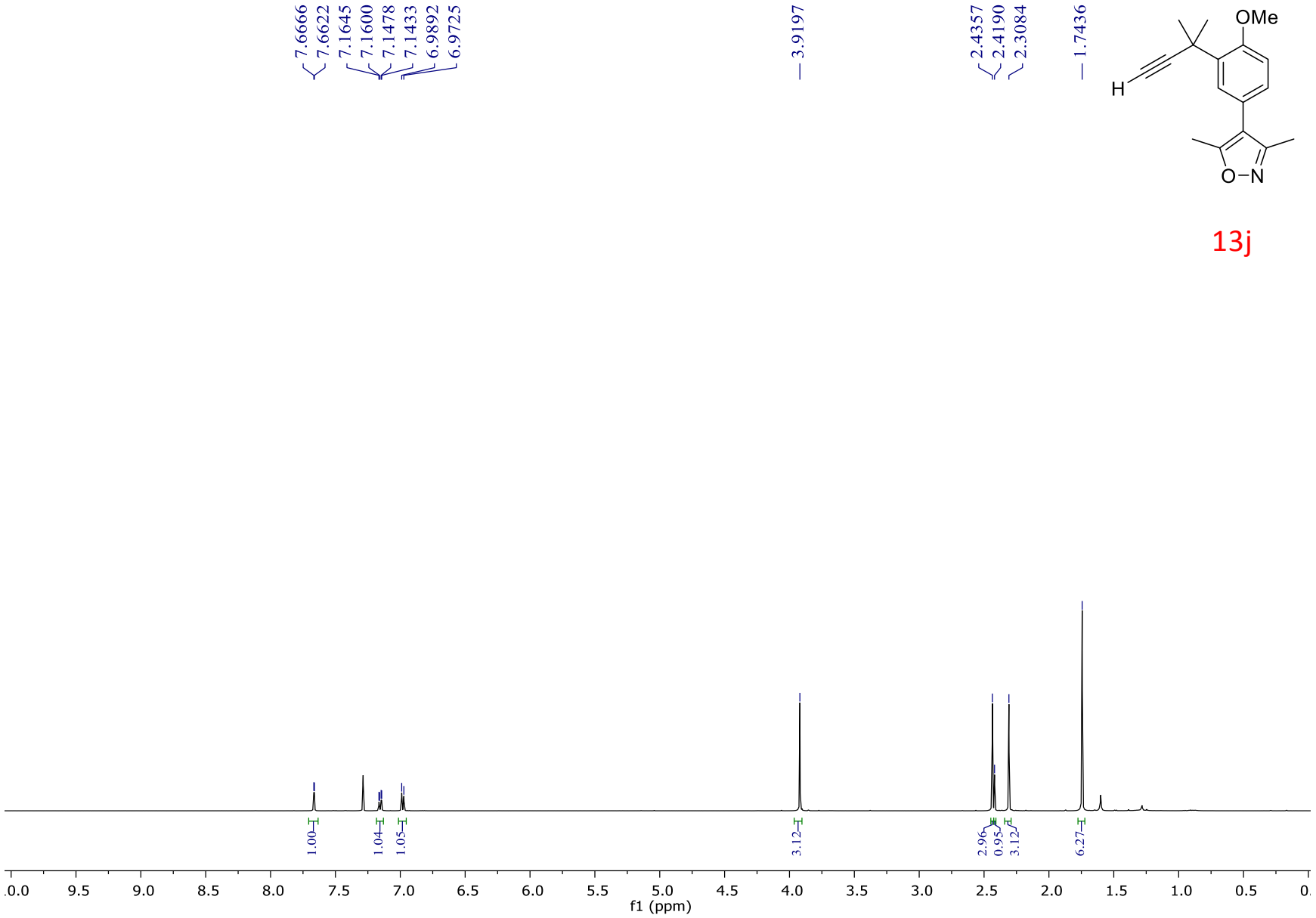
13h



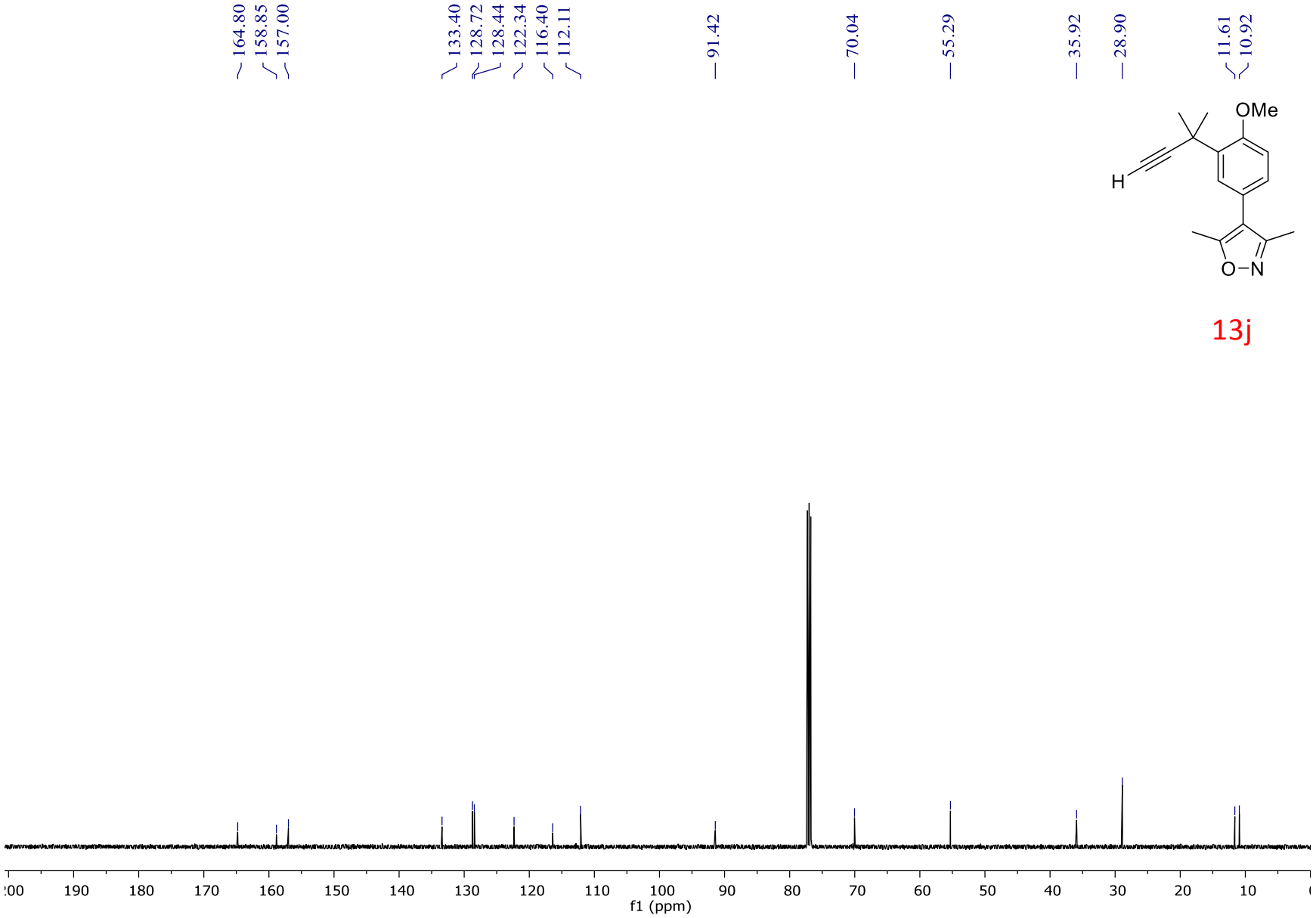

8.6005
7.4631
7.4529
7.3577
7.3502
7.2865
7.0767
7.0692
2.4095
1.7300
S
N
H
1.98
2.06
1.05
1.03
0.85
6.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

13i


154.20
150.29
141.48
139.06
124.93
124.26
119.57
89.54
69.66
33.97
32.44
S
N
H
13i
f1 (ppm)


7.6666
7.6622
7.1645
7.1600
7.1478
7.1433
6.9892
6.9725
3.9197
2.4357
2.4190
2.3084
1.7436
OMe
H
O–N
1.00
1.04
1.05
3.12
2.96
0.95
3.12
6.27
f1 (ppm)

13j


164.80
158.85
157.00
133.40
128.72
128.44
122.34
116.40
112.11
91.42
70.04
55.29
35.92
28.90
11.61
10.92
OMe
H
O–N
13j
f1 (ppm)